passmedicine PART 2

ONCOLOGY

2024

A 20-year-old asymptomatic woman is referred to the genetics clinic. Her grandmother died of breast cancer aged 54 and her mother and older sister have both recently been diagnosed with the disease.

Breast examination does not reveal any lumps and her recent ultrasound of the breasts did not reveal any suspicious lesions.

What should she be told about her breast cancer risk?

- Her chance of having a BRCA1 mutation is 55-65%
- Her chance of having a BRCA2 mutation is 55-65%
- If BRCA1 positive, she has a 55-65% chance of developing breast cancer
- If BRCA2 positive, she has a 55-65% chance of developing breast cancer
- Given her family history, she has a 55-65% chance of developing breast cancer

Submit answer

Reference ranges

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A 20-year-old asymptomatic woman is referred to the genetics clinic. Her grandmother died of breast cancer aged 54 and her mother and older sister have both recently been diagnosed with the disease.

Breast examination does not reveal any lumps and her recent ultrasound of the breasts did not reveal any suspicious lesions.

What should she be told about her breast cancer risk?

Her chance of having a BRCA1 mutation is 55-65%	7%
Her chance of having a BRCA2 mutation is 55-65%	3%
If BRCA1 positive, she has a 55-65% chance of developing breast cancer	49%
If BRCA2 positive, she has a 55-65% chance of developing breast cancer	15%
Given her family history, she has a 55-65% chance of developing breast cancer	25%

The BRCA1 and BRCA2 genes are tumour suppressor genes involved in DNA repair. Familial mutations in these genes are associated with an increased risk of breast and ovarian cancer. Carriers tend to develop these cancers at a younger age as they have an inherited germline mutation of one copy of the gene so only require a 'second hit' of damage to the second copy to inactivate it. BRCA mutations account for 20-25% of hereditary breast cancers and 5-10% of all breast cancer cases, They also account for 15% of all ovarian cancer.

If a woman with at least a 10% risk of breast or ovarian cancer (approximated from family history) will be offered genetic screening. This requires genetic counselling and living relative whose DNA can also be tested for the mutation, otherwise, the chance of identifying the mutation is too low. This has important ethical considerations with regard to consent.

The percentage risk of developing breast cancer by age 70 is 55-65% for BRCA1 and 45% for BRCA2 mutations.

The percentage risk of developing ovarian cancer by age 70 is 40% for BRCA1 and 15% for BRCA2 mutations.

Because of the high risks involved, women with a positive test result may choose to have

enhanced screening for these cancers, prophylactic surgery (bilateral mastectomy and/or bilateral salpingo-oophorectomy) or chemoprevention with hormonal drugs.

References:
Cancer Research UK. Breast Cancer Genes. Updated 25 July 2014. Available at: http://www.cancerresearchuk.org/about-cancer/type/breast-cancer/about/risks/breast-cancer-genes. Accessed 7 July 2015

National Cancer Institute. BRCA1 and BRCA2. Cancer Risk and Genetic Testing. Updated 1 April 2015. Available at: http://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet Accessed 7
July 2015

National Institute for Health and Care Excellence. Information for the Public: Familial Breast Cancer. Updated June 2013. Available at: http://publications.nice.org.uk/familial-breast-cancer-breast-cancer-in-the-family-ifp164/genetic-counselling-and-genetic-testing Accessed 7 July 2015

Discuss (2) Improve

Next question

Breast cancer: risk factors

Predisposing factors

- BRCA1, BRCA2 genes - 40% lifetime risk of breast/ovarian cancer
- 1st degree relative premenopausal relative with breast cancer (e.g. mother)
- nulliparity, 1st pregnancy > 30 yrs (twice risk of women having 1st child < 25 yrs)
- early menarche, late menopause
- combined hormone replacement therapy (relative risk increase * 1.023/year of use), combined oral contraceptive use
- past breast cancer
- not breastfeeding
- ionising radiation
- p53 gene mutations
- obesity
- previous surgery for benign disease (?more follow-up, scar hides lump)

123

Next question

Textbooks

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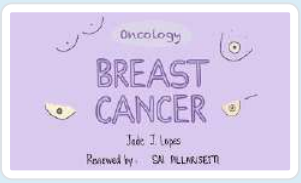
Media



Breast cancer

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Breast cancer

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You are working as a registrar on the palliative care ward. A 58-year-old lady is admitted for symptom control. She has a past medical history of metastatic pancreatic cancer and diabetic nephropathy. She has been suffering from severe abdominal pain which has been unresponsive to titration of morphine, gabapentin and duloxetine.

Blood results are as follows:

Hb	75 g/l	Na^+	138 mmol/l
Platelets	224 * 10^9/l	K^+	3.8 mmol/l
WBC	14.9 * 10^9/l	Urea	18.6 mmol/l
Neuts	12.9 * 10^9/l	Creatinine	288 µmol/l
eGFR	22 mL/min		

You decide to start an opioid which acts as a neuropathic agent by NMDA antagonism. What analgesic is most appropriate?

- Methadone
- Oxycodone
- Buprenorphine
- Paracetamol
- Venlafaxine

Submit answer

Reference ranges

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Neuts	12.9 * 10^9/l	Creatinine	288 µmol/l
eGFR	22 mL/min		

You decide to start an opioid which acts as a neuropathic agent by NMDA antagonism. What analgesic is most appropriate?

Methadone	33%
Oxycodone	15%
Buprenorphine	40%
Paracetamol	0%
Venlafaxine	12%

Methadone can be used as a third line opioid for patients with complex pain that is poorly responsive to other opioids and adjuvants

Important for me Less important

AI

Methadone can be used as a third line opioid for patients with complex pain that is poorly responsive to other opioids and adjuvants. The patients pain has not responded to titration of morphine, combined with two neuropathic adjuvants. Methadone should therefore be considered.

The patients eGFR is les than 30 which also strengthens the decision to start methadone. Opioids which are safe in CKD 4 and 5 include fentanyl, buprenorphine and methadone.

Paracetamol and venlafaxine are not opioids.

Discuss (8) Improve

Next question >

Palliative care prescribing: pain

NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered
- drowsiness is usually transient - if it does not settle then adjustment of the dose should be considered

SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease
    - oxycodone is preferred to morphine in palliative patients with mild-moderate renal impairment
    - if renal impairment is more severe, alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to strong opioids, bisphosphonates or radiotherapy. The assertion that NSAIDs are particularly effective for metastatic bone pain is not supported by studies. Strong opioids have the lowest number needed to treat for relieving the pain and can provide quick relief, in contrast to radiotherapy and bisphosphonates*. All patients, however,

should be considered for referral to a clinical oncologist for consideration of further treatments such as radiotherapy

Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

In addition to strong opioids, bisphosphonates and radiotherapy, denosumab may be used to treat metastatic bone pain.

Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

Conversion between opioids

From	To	Conversion factor
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

The current BNF gives the following conversion factors for transdermal perparations

- a transdermal fentanyl 12 microgram patch equates to approximately 30 mg oral morphine daily
- a transdermal buprenorphine 10 microgram patch equates to approximately 24 mg oral morphine daily.

From	To	Conversion factor
Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

*BMJ 2015;350:h315 Cancer induced bone pain

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***historically a conversion factor of 2 has been used (i.e. oral oxycodone is twice as strong as oral morphine). The current BNF however uses a conversion rate of 1.5

Next question

Textbooks

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Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

3 3

Prescribing opioids in palliative care

Suggest link

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Media

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Understanding The Causes of Pain and Pain Management

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You are asked to provide advice on a patient who has metastatic renal cell carcinoma with pulmonary and bone metastases. They are being managed in their own home with community palliative care input, but their swallow has started to deteriorate. It is now felt that they are approaching the terminal phase of their illness and a decision has been made to start a syringe driver. They report good pain control with their current analgesia regime.

Their current analgesia regime is 60mg oxycodone modified release capsules twice a day with oxycodone instant release, taken as required. The oxycodone modified release is converted into the equivalent subcutaneous dose for an oxycodone syringe driver.

What would be the most appropriate dose of breakthrough analgesia to prescribe based on the current syringe driver dose?

- Oxycodone I/R oral solution 20mg
- Oxycodone I/R oral solution 10mg
- Oxycodone subcutaneous injection 10mg
- Morphine sulphate for injection 10mg
- Morphine sulphate injection 20mg

Submit answer

Reference ranges

Score: **0%**

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Oxycodone I/R oral solution 20mg	33%
Oxycodone I/R oral solution 10mg	10%
Oxycodone subcutaneous injection 10mg	42%
Morphine sulphate for injection 10mg	9%
Morphine sulphate injection 20mg	7%

Breakthrough dose = 1/6th of daily morphine dose

Important for me Less important

The breakthrough dose for analgesia should be one sixth of the total dose administered within 24 hours. If there are no changes to the total dose of oxycodone and it is converted to subcutaneous then the total dose is halved (120mg to 60mg). This is because the subcutaneous strength is twice that of oral oxycodone. The drug choice for breakthrough should match what is in the syringe driver as much as possible (stick with oxycodone) and the breakthrough should be a sixth of the total dose. Given that they need a syringe driver which is made up of oxycodone, the most appropriate drug choice would be subcutaneous oxycodone. Therefore, the breakthrough dose would be a sixth of 60mg= 10mg.

Palliative care prescribing: pain ★

NICE guidelines

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Usually transient	Usually persistent
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123

Next question

Textbooks

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Extended textbook

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NICE

3 1

2012 Opioids in palliative care guidelines

BNF

3 3

Prescribing opioids in palliative care

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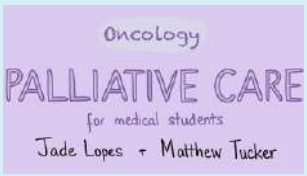
Media



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Understanding The Causes of Pain and Pain Management

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You are looking after a 65-year-old man with a background of high-grade lymphoma who she is currently receiving R-CHOP chemotherapy for. She developed neutropaenic sepsis yesterday for which she was started on piperacillin/tazobactam, and gentamicin. She has been persistently pyrexial for the past 24 hours.

She has a background of complex pain for which she uses a 25micrograms/hour fentanyl patch. You are asked to review her due to confusion and visual hallucinations. On examination, she has pinpoint pupils, GCS 14 (M6, V4, E4), and you note myoclonic jerks.

Na^+	136 mmol/L	(135 - 145)
K^+	3.8 mmol/L	(3.5 - 5.0)
Bicarbonate	19 mmol/L	(22 - 29)
Urea	7.2 mmol/L	(2.0 - 7.0)
Creatinine	130 µmol/L	(55 - 120)

Bilirubin	14 µmol/L	(3 - 17)
ALP	95 u/L	(30 - 100)
ALT	82 u/L	(3 - 40)
Î³GT	86 u/L	(8 - 60)
Albumin	35 g/L	(35 - 50)

You suspect opioid toxicity. What is the most likely explanation for this?

- Acidosis
- Fentanyl and piperacillin/tazobactam drug interaction
- Increased fentanyl absorption due to pyrexia
- Liver dysfunction
- Renal dysfunction

Submit answer

Reference ranges

Score: **0%**

1 -
2 -
3 -
4 -

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You suspect opioid toxicity. What is the most likely explanation for this?

- Acidosis 6%
- Fentanyl and piperacillin/tazobactam drug interaction 11%
- Increased fentanyl absorption due to pyrexia 56%
- Liver dysfunction 12%
- Renal dysfunction 15%

Transdermal fentanyl absorption is increased by heat (e.g. hot water bottle) or pyrexia, potentially leading to opioid toxicity

Important for me Less important

Transdermal fentanyl absorption is increased by heat or pyrexia (which results in vasodilation and increased blood flow), potentially leading to opioid toxicity. This is therefore the correct option.

Acidosis is incorrect. Acidosis is not known to exacerbate opioid toxicity.

Renal dysfunction is incorrect. Fentanyl is hepatically metabolised by CYP450 3A4 with no active metabolites. Therefore it is the opioid of choice in renal failure.

Liver dysfunction is incorrect. Although the patient has a mild transaminitis, their synthetic liver function is normal, making it an unlikely contributing factor.

Piperacillin/tazobactam is incorrect. Fentanyl has no known interactions with piperacillin/tazobactam.

Discuss (4) | Improve

Next question >

Palliative care prescribing: pain

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Opioid side-effects

Usually transient	**Usually persistent**
Nausea Drowsiness	Constipation

Conversion between opioids

From	**To**	**Conversion factor**
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Oral tramadol	Oral morphine	Divide by 10**

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Next question

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Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

3 3

Prescribing opioids in palliative care

Suggest link

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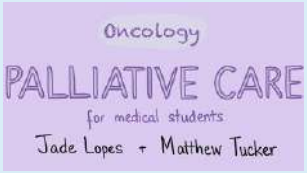
Media



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Understanding The Causes of Pain and Pain Management

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A 63-year-old woman presents with unrelenting thoracic back pain. She finds that the pain is debilitating, especially as she helps look after her grandchildren. She has a past medical history of breast cancer diagnosed two years ago, for which she underwent a mastectomy with reconstruction. She also had postoperative radiotherapy and endocrine therapy. As she was found to be BRCA1 positive, she underwent a hysterectomy with bilateral oophorectomy as well. On examination, she is tender over the spine at T4, but neurological examination is unremarkable. What is the most appropriate imaging investigation for her back pain?

- MRI of the whole spine within 7 days
- MRI of the thoracic spine within 7 days
- MRI of the whole spine within 24 hours
- MRI of the thoracic spine within 24 hours
- Bone scan of the whole body within 7 days

Submit answer

Reference ranges

Score: **0%**

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A 63-year-old woman presents with unrelenting thoracic back pain. She finds that the pain is debilitating, especially as she helps look after her grandchildren. She has a past medical history of breast cancer diagnosed two years ago, for which she underwent a mastectomy with reconstruction. She also had postoperative radiotherapy and endocrine therapy. As she was found to be BRCA1 positive, she underwent a hysterectomy with bilateral oophorectomy as well. On examination, she is tender over the spine at T4, but neurological examination is unremarkable. What is the most appropriate imaging investigation for her back pain?

MRI of the whole spine within 7 days	40%
MRI of the thoracic spine within 7 days	6%
MRI of the whole spine within 24 hours	45%
MRI of the thoracic spine within 24 hours	5%
Bone scan of the whole body within 7 days	4%

The correct answer is MRI whole spine within 7 days. This is a patient with known cancer presenting with highly suspicious back pain but no evidence of spinal cord compression. The most appropriate modality is MRI which can not only detect metastasis but also demonstrate patency or compression of the spinal cord. The whole spine should be scanned as to exclude further metastasis as 30-50% of patients have multi-level involvement by the time of presentation. The timing of the scan depends on suspicion of cord compression. For this patient, there is no evidence of neurological compromise and therefore the scan does not have to occur within 24 hours.

Discuss (4) | Improve

Next question

Spinal metastases

Patients may present with spinal metastases before developing metastatic spinal cord compression. It is, therefore, important to detect these patients early before any neurological compromise develops.

Symptoms and findings

- Unrelenting lumbar back pain
- Any thoracic or cervical back pain
- Worse with sneezing, coughing or straining
- Nocturnal
- Associated with tenderness

If any neurological features are present then spinal cord compression must be suspected and acted on promptly. Without neurological features, a whole spine MRI should be completed within one week. The whole spine should be imaged as patients commonly present with multi-level disease.

Sources:
Al-Qurainy, Rasha, and Emily Collis. 'Metastatic Spinal Cord Compression: Diagnosis and Management.' Bmj (2016): I2539.

Metastatic Spinal Cord Compression in Adults: Risk Assessment, Diagnosis and Management Clinical Guideline [CG75]. National Institute of Clinical Excellence. N.p., Nov. 2008.

Next question

Textbooks

High-yield textbook

Extended textbook

Score: **9.3%**

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You are looking after a 68-year-old man with aggressive multiple myeloma. He has intractable vomiting which has not improved with regular subcutaneous metoclopramide.

Blood results are as follows:

Calcium	4.2 mmol/L	(2.1-2.6)

You decide to start him on a syringe driver. What would be your anti-emetic of choice?

- Aprepitant
- Cyclizine
- Levomepromazine
- Nabilone
- Ondansetron

Submit answer

Reference ranges

Score: **0%**

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You are looking after a 68-year-old man with aggressive multiple myeloma. He has intractable vomiting which has not improved with regular subcutaneous metoclopramide.

Blood results are as follows:

Calcium	4.2 mmol/L	(2.1-2.6)

You decide to start him on a syringe driver. What would be your anti-emetic of choice?

Metabolic causes of nausea and vomiting, for example uraemia and hypercalcaemia, cause nausea and vomiting by stimulating dopamine type 2 (D2) receptors on the chemoreceptor trigger zone. This pathway is most effectively blocked by using a central dopamine antagonist such as haloperidol

Important for me Less important

Metabolic causes of nausea and vomiting (e.g. hypercalcaemia) are particularly sensitive to central dopamine antagonists such as **levomepromazine** making this the favoured choice.

Levomepromazine is a very broad spectrum anti-emetic that acts as an antagonist to multiple receptors including histamine type 1, muscarinic-cholinergic, dopaminergic 2, alpha-1 adrenoceptor, and 5HT-2 receptors. Thus it is a powerful anti-emetic that can be used in many scenarios.

Aprepitant is a substance P/neurokinin 1 receptor antagonist used to prevent chemotherapy-induced and postoperative nausea and vomiting. The patient in this clinical case has nausea secondary to a metabolic abnormality, and thus a dopamine antagonist is the preferred choice.

Cyclizine is a histamine H1-receptor antagonist which may have effects directly on the vestibular system and on the chemoreceptor trigger zone. It also exerts a central anticholinergic action The

patient in this clinical case has nausea secondary to a metabolic abnormality, and thus a dopamine antagonist is the preferred choice.

Ondansetron is a specific 5HT3-receptor antagonist which blocks 5HT3 receptors in the gastrointestinal tract and in the CNS. The patient in this clinical case has nausea secondary to a metabolic abnormality, and thus a dopamine antagonist is the preferred choice.

Nabilone is a synthetic cannabinoid which is used to treat nausea and vomiting caused by cytotoxic chemotherapy, which is unresponsive to conventional antiemetics.

Discuss (3) | Improve

Next question >

Syringe drivers ★

A syringe driver should be considered in the palliative care setting when a patient is unable to take oral medication due to nausea, dysphagia, intestinal obstruction, weakness or coma. In the UK there are two main types of syringe driver:

- Graseby MS16A (blue): the delivery rate is given in mm per hour
- Graseby MS26 (green): the delivery rate is given in mm per 24 hours

The majority of drugs are compatible with water for injection although for the following drugs sodium chloride 0.9% is recommended:

- granisetron
- ketamine
- ketorolac
- octreotide
- ondansetron

Commonly used drugs

- nausea and vomiting: cyclizine, levomepromazine, haloperidol, metoclopramide
- respiratory secretions/bowel colic: hyoscine hydrobromide, hyoscine butylbromide, or glycopyrronium bromide.
- agitation/restlessness: midazolam, haloperidol, levomepromazine
- pain: diamorphine is the preferred opioid

Mixing and compatibility issues

- diamorphine is compatible with the majority of other drugs used including dexamethasone, haloperidol, hyoscine butylbromide, hyoscine hydrobromide, levomepromazine, metoclopramide, midazolam
    - cyclizine may precipitate with diamorphine when given at higher doses

- cyclizine is incompatible with a number of drugs including clonidine, dexamethasone, hyoscine butylbromide (occasional), ketamine, ketorolac, metoclopramide, midazolam, octreotide, sodium chloride 0.9%

123

Next question

Textbooks

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Links

Patient.info

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Syringe drivers

Suggest link

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Score: **9.3%**

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A 54-year-old-man with a history of granulomatosis with polyangiitis attends for his annual review in the rheumatology clinic. He was diagnosed at age 35 where he presented with rapidly progressive glomerulonephritis and pulmonary haemorrhage and was treated with cyclophosphamide and steroids. He required a period of haemofiltration on the intensive care unit but has remained well since.

Today, he feels well after recently quitting smoking but reports occasional blood in his urine. On examination, his abdomen is soft and non tender, there is no pallor or oedema and his chest is clear. His investigations are below and his urine appears clear.

Hb	105 g/l
Platelets	300* 10^9/l
WBC	5* 10^9/l
Urinalysis	blood 3+ protein -
Na^+	139 mmol/l
K^+	4.2 mmol/l
Urea	5.6 mmol/l
Creatinine	98 µmol/l

What is his likely diagnosis?

- Recurrence of glomerulonephritis
- Transitional cell carcinoma
- Renal calculi
- Faulty urinalysis recording
- Rhabdomyolysis

Submit answer

Reference ranges

Score: **0%**

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Urinalysis	blood 3+ protein -
Na^+	139 mmol/l
K^+	4.2 mmol/l
Urea	5.6 mmol/l
Creatinine	98 µmol/l

What is his likely diagnosis?

Recurrence of glomerulonephritis	12%
Transitional cell carcinoma	79%
Renal calculi	4%
Faulty urinalysis recording	3%
Rhabdomyolysis	2%

Use of cyclophosphamide in granulomatosis with polyangiitis is associated with increased risk of bladder cancer

Important for me Less important

The use of cyclophosphamide is linked to transitional cell carcinoma in patients with vasculitis. Given that his U&Es are normal, a recurrence of glomerulonephritis is unlikely. Renal calculi would cause loin to groin pain. Haematuria can often not be visible to the eye even when present. While rhabdomyolysis could give a positive dipstick, there are no other features to suggest this

Discuss (3) Improve

Next question

Cyclophosphamide

Cyclophosphamide is an alkylating agent used in the management of cancer and autoimmune conditions. It works by causing cross-linking of DNA

Adverse effects

- haemorrhagic cystitis: incidence reduced by the use of hydration and mesna
- myelosuppression
- transitional cell carcinoma

Mesna

- 2-**me**rcaptoethane **s**ulfonate **Na**
- a metabolite of cyclophosphamide called acrolein is toxic to urothelium
- mesna binds to and inactivates acrolein helping to prevent haemorrhagic cystitis

123

Next question

Textbooks

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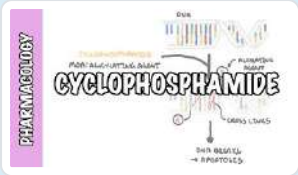
Extended textbook

Media



Cyclophosphamide - pharmacology, mechanism of action, adverse effects

Armando Hasudungan - YouTube

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A 68-year-old man is admitted to the unit with an exacerbation of severe pain around his abdomen. He describes it as a tight band like pain which is burning in character. He has a past medical history of metastatic prostate cancer. His drug history includes morphine modified release (100mg, twice daily), duloxetine (60mg, twice daily), pregabalin (200mg, three times per day). He states that the pain initially responded well to the analgesics he is on however over the past few weeks it has got progressively worse and culminated in a severe attack of pain today.

You suspect that he has got severe neuropathic pain secondary to spinal metastases. The pain is now poorly controlled with a large dose of opioids and two neuropathic agents. Your consultant decides to start him on ketamine.

What acute complication is it important to monitor for?

- Bladder dysfunction
- Liver dysfunction
- Raised intracranial pressure
- Cardiomyopathy
- Pulmonary fibrosis

Submit answer

Reference ranges

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You suspect that he has got severe neuropathic pain secondary to spinal metastases. The pain is now poorly controlled with a large dose of opioids and two neuropathic agents. Your consultant decides to start him on ketamine.

What acute complication is it important to monitor for?

Bladder dysfunction	27%
Liver dysfunction	20%
Raised intracranial pressure	42%
Cardiomyopathy	9%
Pulmonary fibrosis	2%

Ketamine can cause raised intracranial pressure. It is important to monitor for side effects such as headache, papilloedema, and vomiting

Important for me Less important

Ketamine can be used for neuropathic pain poorly responsive to titrated opioids and oral adjuvant analgesics (e.g. antidepressant and/or anticonvulsant) particularly when there is abnormal pain sensitivity (e.g. allodynia, hyperalgesia or hyperpathia). Ketamine is an NMDA receptor antagonists. Side effects to be aware of include hypertension, raised intracranial pressure and hallucinations.

Bladder and liver dysfunction can occur with long term use of ketamine. Therefore, if a patient is anticipated to have a reasonably good prognosis, alternative options should be considered to replace the ketamine, for example lidocaine infusions.

Next question

Syringe drivers

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Next question

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Links

Patient.info

11 12

Syringe drivers

Suggest link

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Score: **9.3%**

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A medical consult was sought from the nursing staff concerning a 68-year-old gentleman admitted with a urinary tract infection. He was diagnosed with terminal adenocarcinoma of the pancreas six months ago. He had complained of increasing severe abdominal pain for the last few weeks for which his GP commenced and then titrated morphine sulphate tablets (MST) achieving a temporary analgesic effect with each increment. By the time of admission he had been using 150mg BD and was unable to tolerate any further dose increases owing to drowsiness.

His drug history comprised of ciprofloxacin 250mg BD started four days ago for the management of urinary tract infection, paracetamol 1g QDS, tramadol 100mg QDS, MST 150mg BD, senna 2 tabs ON & Movicol one sachet BD.

In view of the continuing abdominal pain investigations were organised by the inpatient team revealing the following findings:

Hb	135 g/l
Platelets	224 * 10^9/l
WBC	11.2 * 10^9/l

Bilirubin	23 µmol/l
ALP	189 u/l
ALT	326 u/l
γGT	178 u/l
Albumin	34 g/l

Chest x-ray: Normal heart borders and lung fields, no evidence of subdiaphragmatic air.
Abdominal x-ray: presence of faeces, no evidence of dilatation.
USS abdomen: multiple hypoechoic lesions within the liver, nil else abnormal noted.

What is the next most appropriate management option?

- Commence syringe driver containing diamorphine
- Refer for immediate surgical consult
- Refer for palliative radiotherapy
- Convert MST to fentanyl

Commence trial with dexamethasone

Submit answer

Reference ranges

Score: **0%**

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Chest x-ray: Normal heart borders and lung fields, no evidence of subdiaphragmatic air.
Abdominal x-ray: presence of faeces, no evidence of dilatation.
USS abdomen: multiple hypoechoic lesions within the liver, nil else abnormal noted.

What is the next most appropriate management option?

Commence syringe driver containing diamorphine	20%
Refer for immediate surgical consult	4%
Refer for palliative radiotherapy	10%
Convert MST to fentanyl	19%

Commence trial with dexamethasone 47%

This gentleman has evidence of extensive hepatic metastases most probably arising from known adenocarcinoma of the pancreas. Despite an escalating opiate regimen he is unable to obtain satisfactory pain relief. One of the sources of pain associated with liver metastases is due to stretching and irritation of the liver capsule for which a trial of dexamethasone may provide an analgesic effect. Option 5 is, therefore, the most suitable option.

There is no evidence of obstruction or perforation and thus a surgical consult is not warranted, and palliative radiotherapy is not specifically indicated here (in contrast with bone metastases).

Switching to fentanyl will probably not provide any additional benefit in terms of tolerance compared with MST; it is however indicated in patients with poor renal failure owing to its predominant hepatic route of metabolism. For further information:

http://www.ruh.nhs.uk/ForClinicians/departmentsruh/PalliativeCare/documents/palliativecarehandbook.pd provides a helpful guide for prescribing in palliative settings.

Discuss (5) Improve

Next question >

Palliative care prescribing: pain

NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered
- drowsiness is usually transient - if it does not settle then adjustment of the dose should be considered

SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease
    - oxycodone is preferred to morphine in palliative patients with mild-moderate renal impairment
    - if renal impairment is more severe, alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to strong opioids, bisphosphonates or radiotherapy. The assertion that NSAIDs are particularly effective for metastatic bone pain is not supported by studies. Strong opioids have the lowest number needed to treat for relieving the pain and can provide quick relief, in contrast to radiotherapy and bisphosphonates*. All patients, however, should be considered for referral to a clinical oncologist for consideration of further treatments such as radiotherapy

Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

In addition to strong opioids, bisphosphonates and radiotherapy, denosumab may be used to treat metastatic bone pain.

Opioid side-effects

Usually transient	**Usually persistent**
Nausea Drowsiness	Constipation

Conversion between opioids

From	**To**	**Conversion factor**
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

The current BNF gives the following conversion factors for transdermal perparations

- a transdermal fentanyl 12 microgram patch equates to approximately 30 mg oral morphine daily
- a transdermal buprenorphine 10 microgram patch equates to approximately 24 mg oral morphine daily.

From	To	Conversion factor
Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

*BMJ 2015;350:h315 Cancer induced bone pain

**this has previously been stated as 5 but the current version of the BNF states a conversion of 10

***historically a conversion factor of 2 has been used (i.e. oral oxycodone is twice as strong as oral morphine). The current BNF however uses a conversion rate of 1.5

Next question

Textbooks

High-yield textbook

Extended textbook

Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

3 3

Prescribing opioids in palliative care

Suggest link

Report broken link

Media

Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube

20 2

Understanding The Causes of Pain and Pain Management

Zero To Finals - YouTube

1 1

Report broken media

Score: **9.3%**

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A medical consult was sought regarding a 58-year-old gentleman admitted with pneumonia complaining of relentless hiccups. He was diagnosed with hepatocellular carcinoma six months ago and was deemed not for curative treatment owing to the extent of the disease. He was initially comfortable with no discernible symptoms but over the last four weeks developed hiccups. In conjunction with the palliative care nurse his GP had initially trialled domperidone and then haloperidol but with no improvement in his symptoms. He denied the presence of any other symptoms other than fatigue, and upon questioning denied the presence of abdominal pain, heartburn or early satiety.

His past medical history was comprised of alcohol dependence syndrome, chronic liver disease, hypertension and hypercholesterolaemia for which he was prescribed thiamine 100mg TDS, lactulose 10mls BD, spironolactone 100mg OD, propranolol 40mg OD, simvastatin 20mg OD as well as intravenous co-amoxiclav 625mg TDS for the treatment of his pneumonia.
Examination revealed the presence of a cachectic male. His blood pressure was 108/58 mmHg, heart rate 78 bpm, respiratory rate 18/min and temperature 36.6ºC. Examination of his gastrointestinal system revealed the presence of a palpable mass in the right upper quadrant inferior to the right sterna edge and ascites with no tenderness. Examination of his neurological system revealed the absence of any focal neurological symptoms; likewise, examination of cardiovascular and respiratory systems was unremarkable.

Recent investigations revealed the following results:

Bilirubin	22 µmol/l
ALP	221 u/l
ALT	278 u/l
Protein	62 g/l
Albumin	18 g/l

Chest x-ray: normal heart borders and lung fields

Surveillance upper GI endoscopy four months ago: normal stomach mucosal surface, no evidence of portal hypertension

Which of the following options is the best option with a view to managing his hiccups?

- Commence treatment with proton pump inhibitor
- Commence treatment with levomepromazine

- Commence treatment with dexamethasone
- Commence treatment with midazolam infusion
- Commence treatment with baclofen

Submit answer

Reference ranges

Score: **0%**

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A medical consult was sought regarding a 58-year-old gentleman admitted with pneumonia complaining of relentless hiccups. He was diagnosed with hepatocellular carcinoma six months ago and was deemed not for curative treatment owing to the extent of the disease. He was initially comfortable with no discernible symptoms but over the last four weeks developed hiccups. In conjunction with the palliative care nurse his GP had initially trialled domperidone and then haloperidol but with no improvement in his symptoms. He denied the presence of any other symptoms other than fatigue, and upon questioning denied the presence of abdominal pain, heartburn or early satiety.

His past medical history was comprised of alcohol dependence syndrome, chronic liver disease, hypertension and hypercholesterolaemia for which he was prescribed thiamine 100mg TDS, lactulose 10mls BD, spironolactone 100mg OD, propranolol 40mg OD, simvastatin 20mg OD as well as intravenous co-amoxiclav 625mg TDS for the treatment of his pneumonia.
Examination revealed the presence of a cachectic male. His blood pressure was 108/58 mmHg, heart rate 78 bpm, respiratory rate 18/min and temperature 36.6ºC. Examination of his gastrointestinal system revealed the presence of a palpable mass in the right upper quadrant inferior to the right sterna edge and ascites with no tenderness. Examination of his neurological system revealed the absence of any focal neurological symptoms; likewise, examination of cardiovascular and respiratory systems was unremarkable.

Recent investigations revealed the following results:

Bilirubin	22 µmol/l
ALP	221 u/l
ALT	278 u/l
Protein	62 g/l
Albumin	18 g/l

Chest x-ray: normal heart borders and lung fields

Surveillance upper GI endoscopy four months ago: normal stomach mucosal surface, no evidence of portal hypertension

Which of the following options is the best option with a view to managing his hiccups?

- Commence treatment with proton pump inhibitor — 2%
- Commence treatment with levomepromazine — 38%

Commence treatment with dexamethasone	36%
Commence treatment with midazolam infusion	3%
Commence treatment with baclofen	22%

This gentleman has known advanced hepatocellular carcinoma and is complaining of distressing hiccups. He does not have any sign of gastro-oesophageal reflux and therefore a trial of proton pump inhibitor is unlikely to be of benefit. In the presence of hepatic or cerebral cancer a trial of dexamethasone may induce some remission and is therefore suggested as an appropriate next line given he has already had a trial of treatment with a prokinetic and a typical antipsychotic with no remission; see http://www.palliativecareguidelines.scot.nhs.uk/guidelines/symptom-control/Hiccups.aspx for further information. There is also limited evidence for treatment with baclofen and levomepromazine; subcutaneous midazolam should be reserved if all else proves futile. Note also the BNF has a very useful section regarding prescribing in palliative care scenarios; in this instance it also suggests the use of antacids or nifedipine in addition to the above options.

Discuss (6) | Improve

Next question

Palliative care prescribing: hiccups

Management of hiccups

- chlorpromazine is licensed for the treatment of intractable hiccups
- haloperidol, gabapentin are also used
- dexamethasone is also used, particularly if there are hepatic lesions

123

Next question

Textbooks

High-yield textbook

Extended textbook

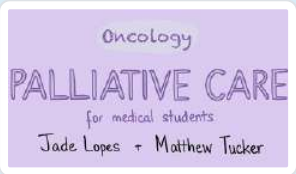
Links

NHS Scotland 7 4

Scottish Palliative Care Guidelines - hiccups

Suggest link Report broken link

Media



Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube 1 2

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A 47-year-old woman presents to the emergency department with sudden onset of shortness of breath and pleuritic chest pain. Observations demonstrate marked hypoxia and she is given oxygen and analgesia and undergoes a chest X-ray followed by a CT pulmonary angiogram which shows a pulmonary embolism. There is also an incidental finding of a nodule suspicious of metastatic disease.

She is started on a treatment dose of low molecular weight heparin and admitted under the medical team for further assessment. During a more detailed history, she explains that she has lost one stone in weight over two months and been feeling progressively more tired as well. She denies any other symptoms. She has a past medical history of asthma and also underwent a caesarean section three years ago. She has two children, of which she breastfed both, and has a long history of use of oral contraceptive use. She is an ex-smoker of 5 pack-years and has minimal alcohol intake. Her grandfather died of prostate cancer, and her sister developed breast cancer at the age of 52.

A complete further examination was completed and no abnormalities were found. Routine blood tests are currently pending, and a flexible bronchoscopy for biopsy of the lung nodule has been arranged. How should this patient be further investigated?

- Tumour markers AFP and hCG, and mammography
- CT abdomen and pelvis, tumour markers AFP and hCG, and a myeloma screen
- Ultrasound abdomen and pelvis, and tumours marker AFP and hCG
- CT abdomen and pelvis, and tumour markers AFP and hCG
- CT abdomen and pelvis, myeloma screen, and colonoscopy

Submit answer

Reference ranges

Score: **0%**

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A complete further examination was completed and no abnormalities were found. Routine blood tests are currently pending, and a flexible bronchoscopy for biopsy of the lung nodule has been arranged. How should this patient be further investigated?

Tumour markers AFP and hCG, and mammography	22%
CT abdomen and pelvis, tumour markers AFP and hCG, and a myeloma screen	21%
Ultrasound abdomen and pelvis, and tumours marker AFP and hCG	5%
CT abdomen and pelvis, and tumour markers AFP and hCG	46%
CT abdomen and pelvis, myeloma screen, and colonoscopy	7%

The correct answer is CT abdomen and pelvis, and tumour markers AFP and hCG. These investigations complete all those recommended by NICE for an unknown primary. This question highlights how to investigate a malignancy of unknown origin. This patient has a likely metastatic disease causing a pulmonary embolism with unclear clinical findings as to the location of the primary malignancy.

NICE recommends the following investigations for all patients:

- FBC, U&E, LFT, calcium, urinalysis, LDH
- Chest X-ray
- CT of chest, abdomen and pelvis
- AFP and hCG

NICE recommends the following investigations for specific patients:

- Myeloma screen (if lytic bone lesions)
- Endoscopy (directed towards symptoms)
- PSA (men)
- CA 125 (women with peritoneal malignancy or ascites)
- Testicular US (in men with germ cell tumours)
- Mammography (in women with clinical or pathological features compatible with breast cancer)

A is incorrect because it does not include CT scanning of the abdomen and pelvis. Mammography is tempting but NICE does not recommend it without any clinical findings which are suggestive of a breast malignancy. B and E are incorrect because a myeloma screen is not indicated without lytic bone lesions. E is also incorrect as colonoscopy should be symptom directed. C is incorrect as US is not an appropriate investigation.

Discuss (7) | Improve

Next question >

Investigating metastatic disease of unknown primary

NICE recommends the following investigations for all patients:

- FBC, U&E, LFT, calcium, urinalysis, LDH
- Chest X-ray
- CT of chest, abdomen and pelvis
- AFP and hCG

NICE recommends the following investigations for specific patients:

- Myeloma screen (if lytic bone lesions)
- Endoscopy (directed towards symptoms)
- PSA (men)
- CA 125 (women with peritoneal malignancy or ascites)
- Testicular US (in men with germ cell tumours)
- Mammography (in women with clinical or pathological features compatible with breast cancer)

Source:
Metastatic Malignant Disease of Unknown Origin in Adults: Diagnosis and Management Clinical guideline [CG 104]. National Institute of Clinical Excellence. N.p., Jul. 2010.

Next question

Textbooks

High-yield textbook

Extended textbook

Links

NICE

0 1

2010 Metastatic malignant disease of unknown primary origin in adults

Suggest link

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Score: **9.3%**

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A 62-year-old lady with metastatic breast cancer is admitted with a general decline. She is found to have a pneumonia and treated with IV fluids and antibiotics. She makes limited improvement with these and antibiotics are stopped. The decision is made to focus on control of her symptoms.

She is started on a syringe driver of morphine sulphate to treat breathlessness and pain related to liver metastases. She then develops nausea and hiccups.

Which medication is the best choice to add to the syringe driver?

- Cyclizine
- Domperidone
- Midazolam
- Metoclopramide
- Ondansetron

Submit answer

Reference ranges

Score: **0%**

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She is started on a syringe driver of morphine sulphate to treat breathlessness and pain related to liver metastases. She then develops nausea and hiccups.

Which medication is the best choice to add to the syringe driver?

Cyclizine, domperidone and ondansetron are anti-emetics, though domperidone does not come in a subcutaneous preparation for syringe driver. Midazolam is an anxiolytic.

Metoclopramide is the first choice to treat hiccup as well as nausea. Other options include baclofen, nifedipine and chlorpromazine.

Reference:
British National Formulary. Guidance on prescribing in palliative care. 2015.

Discuss (4) Improve

Next question

Palliative care prescribing: hiccups

Management of hiccups

- chlorpromazine is licensed for the treatment of intractable hiccups
- haloperidol, gabapentin are also used
- dexamethasone is also used, particularly if there are hepatic lesions

Next question

Textbooks

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Extended textbook

Links

NHS Scotland 7 4

Scottish Palliative Care Guidelines - hiccups

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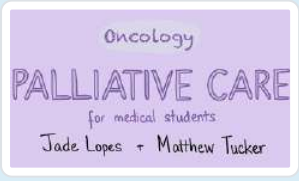
Media



Complete Guide to Palliative Care for Medical Students

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A 60-year-old man has been admitted under urology with difficulty passing urine and back pain. A post-void bladder scan shows 980mls in his bladder. He was catheterised by the admitting doctor and now has haematuria.

He has a background of metastatic prostate cancer, atrial fibrillation, previous NSTEMI, hypertension, hypercholesterolaemia and hypothyroidism. His medications include warfarin and modified-release morphine 30mg every 12 hours.

He has been seen by the urology consultant who has said to put a 3-way catheter in if the haematuria does not settle and refer to the palliative care team for pain management. The palliative care specialist advised increasing the modified release morphine to 45mg every 12 hours.

What dose of immediate-release morphine should the patient be prescribed for breakthrough pain?

- 5mg
- 7.5mg
- 10mg
- 15mg
- 20mg

Submit answer

Reference ranges

Score: **0%**

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He has been seen by the urology consultant who has said to put a 3-way catheter in if the haematuria does not settle and refer to the palliative care team for pain management. The palliative care specialist advised increasing the modified release morphine to 45mg every 12 hours.

What dose of immediate-release morphine should the patient be prescribed for breakthrough pain?

5mg	3%
7.5mg	6%
10mg	10%
15mg	80%
20mg	2%

Breakthrough dose = 1/6th of daily morphine dose

Important for me Less important

To answer this question, you need to calculate the total daily dose of morphine. The amount of immediate-release morphine for breakthrough pain should be one-sixth (1/6) of the total daily dose.

The patient was previously on 60mg of morphine per day. One-sixth of this would be 10mg of immediate-release morphine for breakthrough pain.

The modified release morphine has now been up titrated to 90mg per day. Whenever background morphine is increased, it is important to calculate the new breakthrough pain dosage for patients to receive the maximal benefit. In this case, one-sixth of 90 is 15mg. Therefore the correct answer is 15mg of immediate-release morphine.

Discuss (1) | Improve

Next question >

Palliative care prescribing: pain ★

NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered
- drowsiness is usually transient - if it does not settle then adjustment of the dose should be considered

SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease
    - oxycodone is preferred to morphine in palliative patients with mild-moderate renal impairment
    - if renal impairment is more severe, alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to strong opioids, bisphosphonates or radiotherapy. The assertion that NSAIDs are particularly effective for metastatic bone pain is not supported by studies. Strong opioids have the lowest number needed to treat for relieving the pain and can provide quick relief, in contrast to radiotherapy and bisphosphonates*. All patients, however,

should be considered for referral to a clinical oncologist for consideration of further treatments such as radiotherapy

Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

In addition to strong opioids, bisphosphonates and radiotherapy, denosumab may be used to treat metastatic bone pain.

Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

Conversion between opioids

From	To	Conversion factor
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

The current BNF gives the following conversion factors for transdermal perparations

- a transdermal fentanyl 12 microgram patch equates to approximately 30 mg oral morphine daily
- a transdermal buprenorphine 10 microgram patch equates to approximately 24 mg oral morphine daily.

From	To	Conversion factor
Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

*BMJ 2015;350:h315 Cancer induced bone pain

**this has previously been stated as 5 but the current version of the BNF states a conversion of 10

***historically a conversion factor of 2 has been used (i.e. oral oxycodone is twice as strong as oral morphine). The current BNF however uses a conversion rate of 1.5

Next question

Textbooks

High-yield textbook

Extended textbook

Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

3 3

Prescribing opioids in palliative care

Suggest link

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Media

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Understanding The Causes of Pain and Pain Management

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You are looking after an 82-year-old man with a background of metastatic colorectal carcinoma. He is in significant pain and is on a syringe driver containing 6mg of alfentanil. He has end-stage renal failure.

What breakthrough analgesic will you prescribe?

- 1mg subcutaneous alfentanil
- 25mg subcutaneous morphine
- 25mg subcutaneous oxycodone
- 2mg subcutaneous alfentanil
- 50mg subcutaneous oxycodone

Submit answer

Reference ranges

Score: **0%**

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What breakthrough analgesic will you prescribe?

1mg subcutaneous alfentanil	74%
25mg subcutaneous morphine	4%
25mg subcutaneous oxycodone	12%
2mg subcutaneous alfentanil	7%
50mg subcutaneous oxycodone	2%

Breakthrough dose = 1/6th of daily morphine dose

Important for me Less important

Palliative care guidelines recommend using 1/6 of the daily dose as a breakthrough. Alfentanil is a potent drug and is particularly useful in renal failure as it is metabolised by the liver, has no active metabolites, and has a very short half-life.

Discuss (2) Improve

Next question >

Palliative care prescribing: pain

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Next question

Textbooks

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Extended textbook

Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

3 3

Prescribing opioids in palliative care

Suggest link

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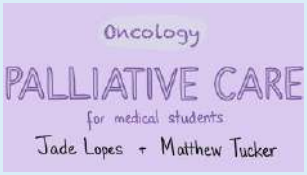
Media



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Understanding The Causes of Pain and Pain Management

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An 82-year-old man is reviewed by the palliative care team on the ward. He has a past medical history of metastatic lung cancer. He is not for any further chemotherapy, surgery or radiotherapy. He has deteriorated rapidly in the prior few days and is considered to be in the last days of life. He is suffering from intractable nausea, the cause of which is not clear.

What is the most appropriate medication to manage his symptoms?

- Buscopan
- Levomepromazine
- Metoclopramide
- Morphine
- Ondansetron

Submit answer

Reference ranges

Score: **0%**

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What is the most appropriate medication to manage his symptoms?

Buscopan	1%
Levomepromazine	55%
Metoclopramide	18%
Morphine	3%
Ondansetron	22%

Levomepromazine is a 'dirty drug' which blocks lots of different receptors (e.g. ACh, DA, 5HT). It is therefore a broad spectrum anti-emetic. It is first line in the last days of life.

Important for me Less important

Levomepromazine is correct. This is a broad-spectrum anti-emetic - a 'dirty drug' targeting many receptors. It is therefore the most suitable choice where the cause of nausea is unknown and in the last days of life.

Buscopan is incorrect. This is indicated in palliative care for excess secretions rather than nausea.

Metoclopramide is incorrect. This would be a rational choice for nausea due to gastric stasis. However, where the cause is unknown and in the last days of life, a more broad spectrum anti-emetic is preferred. Therefore, levomepromazine is preferable.

Morphine is incorrect. This is indicated in palliative care for breathlessness and pain rather than nausea.

Ondansetron is incorrect. This is a rational choice for chemotherapy or post-operative related nausea. However, it is a specific serotonin 5-HT3 receptor antagonist, with a low affinity for dopamine receptors and therefore has a more narrow spectrum of action than levomepromazine and is, therefore, less preferable in this circumstance.

Syringe drivers

A syringe driver should be considered in the palliative care setting when a patient is unable to take oral medication due to nausea, dysphagia, intestinal obstruction, weakness or coma. In the UK there are two main types of syringe driver:

- Graseby MS16A (blue): the delivery rate is given in mm per hour
- Graseby MS26 (green): the delivery rate is given in mm per 24 hours

The majority of drugs are compatible with water for injection although for the following drugs sodium chloride 0.9% is recommended:

- granisetron
- ketamine
- ketorolac
- octreotide
- ondansetron

Commonly used drugs

- nausea and vomiting: cyclizine, levomepromazine, haloperidol, metoclopramide
- respiratory secretions/bowel colic: hyoscine hydrobromide, hyoscine butylbromide, or glycopyrronium bromide.
- agitation/restlessness: midazolam, haloperidol, levomepromazine
- pain: diamorphine is the preferred opioid

Mixing and compatibility issues

- diamorphine is compatible with the majority of other drugs used including dexamethasone, haloperidol, hyoscine butylbromide, hyoscine hydrobromide, levomepromazine, metoclopramide, midazolam
  - cyclizine may precipitate with diamorphine when given at higher doses
- cyclizine is incompatible with a number of drugs including clonidine, dexamethasone, hyoscine butylbromide (occasional), ketamine, ketorolac, metoclopramide, midazolam, octreotide, sodium chloride 0.9%

Textbooks

High-yield textbook

Extended textbook

Links

Patient.info

11 12

Syringe drivers

Suggest link

Report broken link

Score: **9.3%**

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A 65-year-old woman presents to the emergency department with reduced consciousness. Her husband reports that she has been unwell for the past 3 days with coryzal symptoms. She has a past medical history of hypertension and metastatic pancreatic cancer for which she is under the palliative care team. Her regular medications include amlodipine, bisoprolol, paracetamol and a fentanyl patch for pain.

On examination, her temperature is 38.1ºC with a heart rate of 101 beats/min and a blood pressure of 118/66mmHg. Auscultation of the chest is clear with a respiratory rate of 8 breaths/min and oxygen saturations of 92% on air. Her abdomen is soft and non-tender and she is visibly jaundiced. She has a GCS of 11/15 (E2V4M5).

What is the most likely cause of this patient's reduced consciousness?

- Delirium
- Hepatic encephalopathy
- Hypoglycaemia
- Meningitis
- Opioid toxicity

Submit answer

Reference ranges

Score: **0%**

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What is the most likely cause of this patient's reduced consciousness?

Delirium	8%
Hepatic encephalopathy	16%
Hypoglycaemia	2%
Meningitis	3%
Opioid toxicity	72%

Transdermal fentanyl absorption is increased by heat (e.g. hot water bottle) or pyrexia, potentially leading to opioid toxicity

Important for me Less important

Opioid toxicity is correct. This patient has signs of opioid toxicity including drowsiness and a slow respiratory rate. There are multiple differential diagnoses for an acutely unresponsive patient and, therefore, it is key to take a thorough history and examination. From this patient's collateral history it is learned that she uses a fentanyl patch for pain control. It is important to note that transdermal fentanyl absorption is increased by heat whether that be secondary to the application of a hot water bottle or pyrexia. This patient has a fever of 38.1ºC which is a likely contributing factor to her toxicity.

Delirium is incorrect. This is a very reasonable differential diagnosis given the history of fever in a patient with a frail comorbid status. However, delirium is less likely to cause this patient's reduced

respiratory rate compared to opioid toxicity. Generally, fever is associated with tachypnoea and the opposite response should raise suspicion.

Hepatic encephalopathy is incorrect. Although this patient is jaundiced, it is likely to be cholestatic jaundice secondary to the underlying malignancy rather than decompensated liver disease. Furthermore, the acute onset of symptoms and lack of signs of hepatic encephalopathy makes the diagnosis less likely.

Hypoglycaemia is incorrect. This is an important differential diagnosis given the history of advanced malignancy and the likelihood of reduced oral intake. However, the presence of bradypnoea and opioid use makes opioid toxicity more likely.

Meningitis is incorrect. Fever and reduced consciousness are features of meningitis. However, the presence of bradypnoea and the use of strong opioid analgesics make opioid toxicity more likely.

👍 | 👎 | 💬 Discuss (2) | Improve

Next question ›

Palliative care prescribing: pain ★

NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered
- drowsiness is usually transient - if it does not settle then adjustment of the dose should be considered

SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease
    - oxycodone is preferred to morphine in palliative patients with mild-moderate renal impairment
    - if renal impairment is more severe, alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to strong opioids, bisphosphonates or radiotherapy. The assertion that NSAIDs are particularly effective for metastatic bone pain is not supported by studies. Strong opioids have the lowest number needed to treat for relieving the pain and can provide quick relief, in contrast to radiotherapy and bisphosphonates*. All patients, however, should be considered for referral to a clinical oncologist for consideration of further treatments such as radiotherapy

Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

In addition to strong opioids, bisphosphonates and radiotherapy, denosumab may be used to treat metastatic bone pain.

Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

Conversion between opioids

From	To	Conversion factor
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

The current BNF gives the following conversion factors for transdermal perparations

- a transdermal fentanyl 12 microgram patch equates to approximately 30 mg oral morphine daily
- a transdermal buprenorphine 10 microgram patch equates to approximately 24 mg oral morphine daily.

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Oral morphine	Subcutaneous morphine	Divide by 2
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*BMJ 2015;350:h315 Cancer induced bone pain

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Next question

Textbooks

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Extended textbook

Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

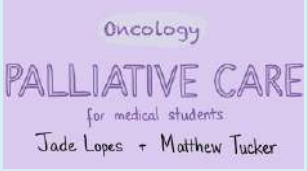
3 3

Prescribing opioids in palliative care

Suggest link

Report broken link

Media



Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube

20 2

Understanding The Causes of Pain and Pain Management

Zero To Finals - YouTube

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Score: **9.3%**

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A 56-year-old man with metastatic small cell lung carcinoma is admitted to hospital with vomiting, ankle swelling and pruritus. He recently completed a course of palliative chemotherapy. He has a background of chronic obstructive pulmonary disease and hypertension and takes morphine sulphate (MST) for pain relief.

On examination, he is cachectic with peripheral oedema and skin excoriations. Heart rate is 96 beats per minute and blood pressure is 140/85 mmHg.

Tests show:

Hb	134 g/l
Platelets	185 * 10^9/l
WBC	5.5 * 10^9/l

Na^+	146 mmol/l
K^+	5.4 mmol/l
Urea	23 mmol/l
Creatinine	420 µmol/l

Urine dip:	Blood +
Urine osmolality	350 mOsm/L
Urinary sodium	45 mEqL
Microscopy:	red cells; casts.

What is the most appropriate pain relief for this patient?

- Fentanyl patch
- Diamorphine
- Oxycodone
- Pregabalin
- Tramadol

Submit answer

Reference ranges

Score: **0%**

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Urine dip:	Blood +
Urine osmolality	350 mOsm/L
Urinary sodium	45 mEqL
Microscopy:	red cells; casts.

What is the most appropriate pain relief for this patient?

Fentanyl patch	56%
Diamorphine	5%
Oxycodone	36%
Pregabalin	1%
Tramadol	1%

This patient has an acute kidney injury secondary to cisplatin chemotherapy. As a result, he needs adjustments to his pain relief. He is on regular, long-acting MST, so the most appropriate substitution is a fentanyl patch.

Oxycodone can be used in moderate renal failure, but only as breakthrough pain relief. Modified release preparations should be avoided. Diamorphine and tramadol should be avoided in renal failure. Pregabalin can be administered at reduced dose, but would not be an appropriate first-line substitution for MST.

Alfentanil and methadone are safe even in severe renal impairment and are administered subcutaneously. Alfentanil would be appropriate for this patient if he had unstable pain and required dose titration.

Discuss (7) | Improve

Next question >

Palliative care prescribing: pain ★

NICE guidelines

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Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

In addition to strong opioids, bisphosphonates and radiotherapy, denosumab may be used to treat metastatic bone pain.

Opioid side-effects

Usually transient	**Usually persistent**
Nausea Drowsiness	Constipation

Conversion between opioids

From	**To**	**Conversion factor**
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	**To**	**Conversion factor**
Oral morphine	Oral oxycodone	Divide by 1.5-2***

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- a transdermal buprenorphine 10 microgram patch equates to approximately 24 mg oral morphine daily.

From	To	Conversion factor
Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

*BMJ 2015;350:h315 Cancer induced bone pain

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Next question

Textbooks

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Extended textbook

Links

NICE

3 1

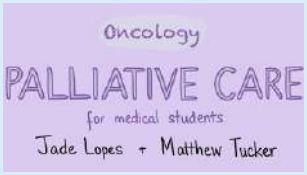
2012 Opioids in palliative care guidelines

BNF 3 3

Prescribing opioids in palliative care

Suggest link Report broken link

Media



Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube 20 2

Understanding The Causes of Pain and Pain Management

Zero To Finals - YouTube 1 1

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Score: **9.3%**

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A 69-year-old male patient presents with worsening mouth soreness and painful swallowing, progressively getting worse over the last week. He started radical radiotherapy for a base of mouth squamous cell cancer three weeks ago. He also has a PEG in situ. He was recently seen by the dietician and is now having fluid and Ensure nutritional supplements via his PEG. He had been given soluble paracetamol by the specialist nurse, but this has failed to control his pain.

On examination, his oral cavity appears inflamed with multiple small ulcers posterior to his lower lip. There are no patches or plaques inside. You change the paracetamol to liquid co-codamol and give him a topical lidocaine gel at 2% strength. What is the most appropriate next step in management to control his symptoms?

- Benzydamine mouthwash
- Menthol mouthwash
- Chlorhexidine mouthwash
- Fluconazole
- Metronidazole

Submit answer

Reference ranges

Score: **0%**

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Benzydamine mouthwash	60%
Menthol mouthwash	2%
Chlorhexidine mouthwash	31%
Fluconazole	6%
Metronidazole	1%

The correct answer is benzydamine mouthwash. This gentleman is suffering from radiotherapy-induced mucositis. Given the location of his tumour and the high dose of radiotherapy necessary for curative therapy, mucositis is not an uncommon side effect. Many of these patients will have a PEG inserted prophylactically in anticipation of the difficulties in maintaining an oral diet with mucositis and oesophageal involvement. For this patient, already on co-codamol, benzydamine mouthwash can be very helpful in treating his symptoms. Menthol and chlorhexidine mouthwashes, often bought over the counter, would increase oral irritation. There is no evidence of fungal or bacterial infection currently.

Discuss (6) | Improve

Next question >

Radiotherapy-induced mucositis

Many patients will suffer from mucositis following radiotherapy to the head and neck. Often these patients will have a PEG tube inserted prior to treatment to help maintain oral intake. Management of pain involves topical treatment such as local anaesthetic gels and benzydamine mouthwashes. Standard WHO based pain ladder should be followed, but medications should be in liquid form.

Sources:
Peterson, D. E., C. B. Boers-Doets, R. J. Bensadoun, and J. Herrstedt. 'Management of Oral and Gastrointestinal Mucosal Injury: ESMO Clinical Practice Guidelines for Diagnosis, Treatment, and Follow-up.' Ann Oncol Annals of Oncology 26.Suppl 5 (2015): V139-151.

Tanay, T., R. Logan, D. Riesenbeck, and A. Hovan. 'Mouth Care Guidance and Support in Cancer and Palliative Care.' UK Oral Mucositis in Cancer Group (2015): n. pag.

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Next question

Textbooks

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A 75-year-old man is admitted to the palliative care unit for end of life care. He has a past medical history of metastatic prostate cancer. His drug history includes a syringe driver with morphine, levomepromazine and midazolam. During personal care the nurses have stated that he suffers excruciating pain when being turned onto his side. His pain throughout the day is otherwise well controlled.

What is the most appropriate way to manage his pain?

- Titrate the syringe driver morphine
- Morphine sulphate modified release tablets
- Oxycodone modified release tablets
- Morphine sulphate immediate release liquid
- Paracetamol

Submit answer

Reference ranges

Score: **0%**

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What is the most appropriate way to manage his pain?

Titrate the syringe driver morphine	15%
Morphine sulphate modified release tablets	7%
Oxycodone modified release tablets	2%
Morphine sulphate immediate release liquid	74%
Paracetamol	2%

Incident pain is defined as pain which comes on as a result of an action or activity, for example during personal care. Sublingual fentanyl has rapid onset and is a short-acting opioid, and is therefore a good choice for treating this type of pain

Important for me Less important

Incident pain is defined as pain which comes on as a result of an action or activity, for example during personal care. Sublingual fentanyl has rapid onset and is a short-acting opioid, and is therefore a good choice for treating this type of pain. Similarly, morphine sulphate immediate release liquid is also suitable.

The patients pain during the day is otherwise well controlled therefore titrating up the syringe driver with more morphine is not appropriate. Not only will this not be particularly effective at treating the incident pain, it will also give rise to unnecessary side effects such as sedation and constipation.

Similarly, morphine sulphate modified release tablets have an action time of approximately 12 hours so they are therefore inappropriate for breakthrough pain as they will cause accumulation of morphine in the system predisposing to toxicity.

Palliative care prescribing: pain ★

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Other points

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Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

Conversion between opioids

From	To	Conversion factor
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

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From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

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Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

*BMJ 2015;350:h315 Cancer induced bone pain

**this has previously been stated as 5 but the current version of the BNF states a conversion of 10

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123

Next question

Textbooks

High-yield textbook

Extended textbook

Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

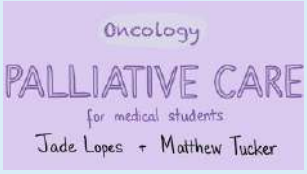
3 3

Prescribing opioids in palliative care

Suggest link

Report broken link

Media



Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube

20 2

Understanding The Causes of Pain and Pain Management

Zero To Finals - YouTube 1 1

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Score: **9.3%**

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Back to top

A 64-year-old cachectic lady presents to the emergency department with difficulty in breathing. She reports smoking since she was 14 years old. Chest X-Ray reveals a large right sided pleural effusion. A sample is obtained under ultrasound-guidance for evaluation. CT does not identify a cause. The results of the pleural aspiration demonstrate an exudative effusion and histology is suggestive of an adenocarcinoma with positive TTF-1 stain. What is the most likely cause for the effusion?

- Non-small cell lung cancer
- Small cell lung cancer
- Ovarian carcinoma
- Breast carcinoma
- Mesothelioma

Submit answer

Reference ranges

Score: **0%**

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Non-small cell lung cancer	43%
Small cell lung cancer	17%
Ovarian carcinoma	24%
Breast carcinoma	5%
Mesothelioma	10%

TTF-1 (thyroid transcription factor 1) is a protein which regulates the transcription of genes specific for the thyroid and lung. Lung adenocarcinomas and small cell carcinomas are usually TTF-1 positive. The histology in the above example is suggestive of an adenocarcinoma and therefore this is mostly likely a lung primary given the TTF-1 stain and history of smoking.

Non-small cell lung cancers include adenocarcinoma, large cell and squamous cell carcinoma.

Discuss (5) | Improve

Next question >

Lung cancer: non-small cell

There are three main subtypes of non-small cell lung cancer:

Squamous cell cancer

- typically central
- associated with parathyroid hormone-related protein (PTHrP) secretion → hypercalcaemia
- strongly associated with finger clubbing
- cavitating lesions are more common than other types
- hypertrophic pulmonary osteoarthropathy (HPOA)

Adenocarcinoma

- typically peripheral
- most common type of lung cancer in non-smokers, although the majority of patients who develop lung adenocarcinoma are smokers

Large cell lung carcinoma

- typically peripheral
- anaplastic, poorly differentiated tumours with a poor prognosis
- may secrete β-hCG

123

Next question

Textbooks

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Extended textbook

Links

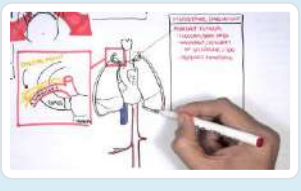
Radiopaedia

4 3

Lung cancer review

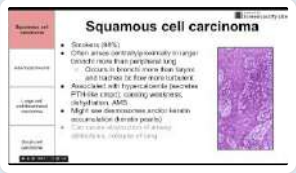
Suggest link Report broken link

Media



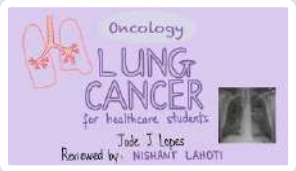
Lung cancer

Armando Hasudungan - YouTube 1 0



Cancers of the lung

MedLecturesMadeEasy - YouTube 1 0



Lung cancer

MedFlix - YouTube 0 0

Lung Cancer: An Overview

Oncology for Medical Students - YouTube 0 0

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Score: **9.3%**

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A 76-year-old woman with metastatic transitional cell carcinoma of the bladder is admitted to hospice with a 3-day history of hallucinations, confusion and pruritus. Her only other symptoms are intermittent vomiting and pelvic discomfort. She has a past medical history of hypertension and has recently completed a course of radiotherapy for bone metastases. She takes paracetamol, morphine sulphate, cyclizine, dexamethasone and a herbal flower remedy for anxiety.

On examination, she is cachectic and frail. The lungs are clear and heart sounds are normal. Pulse rate is 85 beats per minute and blood pressure 130/80mmHg. She is afebrile.

Neurological examination reveals myoclonus. She is mildly hypotonic and all reflexes are diminished. There is miosis on cranial nerve examination.

Blood tests show:

Hb	12.1 g/dl
Platelets	250 * 10^9/l
WBC	12 * 10^9/l

Na^+	135 mmol/l
K^+	4.3 mmol/l
Urea	5 mmol/l
Creatinine	80 µmol/l
Calcium (unadjusted)	2.1 mmol/l

Bilirubin	15 µmol/l
ALP	45 u/l
ALT	15 u/l
AST	20 u/l
Albumin	28 g/l

Urine dip: no abnormality

What is the most likely diagnosis?

- Hypercalcaemia

- Opioid toxicity
- Sepsis
- Corticosteroid psychosis
- Brain metastases

Submit answer

Reference ranges

Score: **0%**

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Bilirubin	15 µmol/l
ALP	45 u/l
ALT	15 u/l
AST	20 u/l
Albumin	28 g/l

Urine dip: no abnormality

What is the most likely diagnosis?

Hypercalcaemia 8%

Opioid toxicity	60%
Sepsis	1%
Corticosteroid psychosis	16%
Brain metastases	15%

This lady is presenting with opioid toxicity. She has vomiting, confusion, hallucinations and pruritus. Her symptoms have been precipitated by a reduction in her opioid requirement. This is a common occurrence in patients who have radiotherapy for bone metastases if their medication dose is not adjusted.

Hypercalcaemia could cause a similar presentation, but the corrected calcium is 2.4 mmol/L. This lady is hypoalbuminaemic due to her advanced cancer. The patient no symptoms of infection. She is apyrexial and her slightly raised white cell count is due to her advanced disease and dexamethasone treatment. Corticosteroid psychosis is possible, but would not cause the neurological signs or pruritus. Transitional cell carcinomas of the urothelial tract only rarely metastasise to the brain; the neurological signs suggest opioid toxicity rather than a focal lesion.

Discuss (5) | Improve

Next question

Palliative care prescribing: pain

NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered

- drowsiness is usually transient - if it does not settle then adjustment of the dose should be considered

SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease
    - oxycodone is preferred to morphine in palliative patients with mild-moderate renal impairment
    - if renal impairment is more severe, alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to strong opioids, bisphosphonates or radiotherapy. The assertion that NSAIDs are particularly effective for metastatic bone pain is not supported by studies. Strong opioids have the lowest number needed to treat for relieving the pain and can provide quick relief, in contrast to radiotherapy and bisphosphonates*. All patients, however, should be considered for referral to a clinical oncologist for consideration of further treatments such as radiotherapy

Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

In addition to strong opioids, bisphosphonates and radiotherapy, denosumab may be used to treat metastatic bone pain.

Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

Conversion between opioids

From	To	Conversion factor
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

The current BNF gives the following conversion factors for transdermal perparations

- a transdermal fentanyl 12 microgram patch equates to approximately 30 mg oral morphine daily
- a transdermal buprenorphine 10 microgram patch equates to approximately 24 mg oral morphine daily.

From	To	Conversion factor
Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

*BMJ 2015;350:h315 Cancer induced bone pain

**this has previously been stated as 5 but the current version of the BNF states a conversion of 10

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Next question

Textbooks

High-yield textbook

Extended textbook

Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

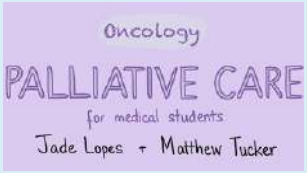
3 3

Prescribing opioids in palliative care

Suggest link

Report broken link

Media



Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube

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Understanding The Causes of Pain and Pain Management

Zero To Finals - YouTube

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Score: **9.3%**

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A 65-year-old man is referred to the oncology team after presenting to the emergency department. The patient described a three-week history of progressive thoracic back pain. The pain was localised to a point between the patient's shoulder blades, and was exacerbated by movement and coughing.

In addition, over the previous 6 hours, the patient reported that he had been struggling to stand up unassisted, and was having difficultly walking. The sudden change in his mobility had been the event that had prompted his attendance at hospital. When questioned directly, the patient described intermittent tingling sensations in his lower legs, but denied any loss of sensation. There had been no dysfunction of his bladder or bowels.

The patient had been diagnosed with prostate cancer five years previously. This had been treated with a radical prostatectomy and hormone therapy. The patient had moved area two years previously, and had subsequently been lost to urological follow-up. Despite his previous cancer treatment, the patient stated that he was very fit and active, playing golf three times a week and taking an active role in the care of his grandchildren.

Peripheral nerve examination of lower limbs: tone generally increased bilaterally; power generally slightly reduced (4+/5) bilaterally; normal coordination; no impairment of light touch or sharp touch sensation; knee and ankle jerks brisk bilaterally, plantar responses up going bilaterally.

Digital rectal examination: preserved peri-anal sensation and normal tone.

Bed-side bladder scan: 50 ml

MRI whole spine: metastatic invasion and collapse of T10 vertebral with spinal cord compression.

The patient was treated with analgesia and dexamethasone while definitive treatment was planned.

What is most appropriate first-line treatment of patient's spinal cord compression?

- Surgical tumour resection and spinal cord stabilisation with adjuvant radiotherapy
- Radiotherapy: single dose 8 Gy
- Chemotherapy: docetaxel
- Best supportive care

Chemotherapy: cabazitaxel

Submit answer

Reference ranges

Score: **0%**

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Bed-side bladder scan: 50 ml

MRI whole spine: metastatic invasion and collapse of T10 vertebral with spinal cord compression.

The patient was treated with analgesia and dexamethasone while definitive treatment was planned.

What is most appropriate first-line treatment of patient's spinal cord compression?

Surgical tumour resection and spinal cord stabilisation with adjuvant radiotherapy	55%
Radiotherapy: single dose 8 Gy	39%
Chemotherapy: docetaxel	2%
Best supportive care	4%

Chemotherapy: cabazitaxel 1%

The best predictor of neurological outcome with treatment in metastatic spinal cord compression is neurological status at the initiation of treatment. The patient in the question has presented very promptly and has only limited neurological compromise. Therefore, it is imperative that definitive treatment is provided promptly (ideally, within 24 hours) to optimise long-term outcome.

Definite treatment of metastatic spinal cord compression can include any combination of radiotherapy, surgery and chemotherapy. Recent evidence indicates that surgery is superior to radiotherapy in retaining or regaining neurological function and relieving pain. In the case of this patient, who has an excellent performance status, surgery followed by radiotherapy would likely offer a better outcome than radiotherapy alone.

Radiotherapy may be considered as first-line treatment in some circumstances. Recommended regimen vary, for example 20 Gy in five daily fractions. The radiotherapy regime offered as a answer to the question would be appropriate as palliative treatment for pain-control, making it an incorrect answer for this patient.

Chemotherapy have a role in the management of spinal-cord compression secondary to chemo-sensitive malignancies (for example, small-cell lung cancer or germ cell tumours), but would not be optimal treatment for this patient.

Al-Qurainy, Collis E. Metastatic spinal cord compression: diagnosis and management. BMJ 2016;353:i2539.

Discuss (5) Improve

Next question >

Neoplastic spinal cord compression

Spinal cord compression is an oncological emergency and affects up to 5% of cancer patients. Extradural compression accounts for the majority of cases, usually due to vertebral body metastases. It is more common in patients with lung, breast and prostate cancer

Features

- back pain
  - the earliest and most common symptom
  - may be worse on lying down and coughing
- lower limb weakness
- sensory changes: sensory loss and numbness
- neurological signs depend on the level of the lesion. Lesions above L1 usually result in upper motor neuron signs in the legs and a sensory level. Lesions below L1 usually cause lower

motor neuron signs in the legs and perianal numbness. Tendon reflexes tend to be increased below the level of the lesion and absent at the level of the lesion

Investigation

- urgent MRI: the 2019 NICE guidelines recommend a whole MRI spine within 24 hours of presentation

Management

- high-dose oral dexamethasone
- urgent oncological assessment for consideration of radiotherapy or surgery

Next question

Textbooks

High-yield textbook

Extended textbook

Links

St Luke's Alliance 7 9

Suspected metastatic spinal cord compression pathway

NICE 7 1

2008 Metastatic spinal cord compression guidelines

Suggest link Report broken link

Media

Spinal Cord - Clinical Anatomy and Physiology (dermatomes, blood supply, shingles, lumbar puncture)

Armando Hasudungan - YouTube

2 0

Spinal Cord Compression

Armando Hasudungan - YouTube

1 0

Metastatic spinal cord compression

Oncology for Medical Students - YouTube

2 1

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Score: **9.3%**

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A 56-year-old patient presents to hospital with confusion. He is a long-term smoker. He has a past-medical history of chronic obstructive pulmonary disease, hypertension, bipolar disease and long-term muscular back pain.

On examination he is confused with a Glasgow Coma Scale score of 14 out of 15. He has a pulse rate of 97 beats per minute with a blood pressure of 145/97 mmHg. Respiratory rate is 14 per minute with oxygen saturations of 95% on room air. He has bilateral vesicular breath sounds on auscultation with normal percussion. His abdomen is soft and non-tender with no masses. He has no focal neurology.

Investigations

Hb	102 g/dL
WCC	8.2 *10^9/l
Platelets	133 *10^9/l

Na+	146 mmol/L
K+	5.4 mmol/L
Cr	132 µmol/L
Ur	10.1 mmol/L

Albumin	26 g/L
Adjusted Calcium	3.78 mmol/L
Alkaline Phosphatase	76 IU/L
PTH	Undetectable
Serum ACE	45U/L (10-50)
Serum Electrophoresis	IgG 18 g/L (5-13 g/L) - Polyclonal
Urinary Electrophoresis	Undetectable

Chest X-ray	Right parahilar opacification 3x4cm
Lumbar Spine X-ray	Normal

What is the likely underlying diagnosis?

- Squamous Cell Carcinoma
- Multiple Myeloma
- Sarcoidosis
- Drug induced hypercalcaemia
- Prostate carcinoma

Submit answer

Reference ranges

Score: **0%**

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Urinary Electrophoresis	Undetectable

Chest X-ray	Right parahilar opacification 3x4cm
Lumbar Spine X-ray	Normal

What is the likely underlying diagnosis?

Squamous Cell Carcinoma	63%
Multiple Myeloma	22%
Sarcoidosis	13%
Drug induced hypercalcaemia	1%
Prostate carcinoma	1%

The patient has severe hypercalcaemia. The commonest causes are hyperparathyroidism and cancer. The patient has a normal alkaline phosphatase without evidence of fracture or bone disease making bone metastases unlikely. The patient has a normal serum ACE with an atypical chest X-ray for sarcoidosis, although unilateral chest findings are possible.

The patient has features of multiple myeloma including anaemia, renal insufficiency and hypercalcaemia. However, there is a polyclonal, rather than a monoclonal increase in paraprotein.

The chest x-ray findings with a background of smoking suggest an underlying respiratory malignancy. This patient has squamous cell carcinoma of the lung with parathyroid related protein secretion causing hypercalcaemia. PrPTH is not deteced on a PTH assay. Hypercalcaemia can induce confusion and renal impairment.

Discuss (9) | Improve

Next question >

Lung cancer: non-small cell ★

There are three main subtypes of non-small cell lung cancer:

Squamous cell cancer

- typically central
- associated with parathyroid hormone-related protein (PTHrP) secretion → hypercalcaemia
- strongly associated with finger clubbing
- cavitating lesions are more common than other types
- hypertrophic pulmonary osteoarthropathy (HPOA)

Adenocarcinoma

- typically peripheral
- most common type of lung cancer in non-smokers, although the majority of patients who develop lung adenocarcinoma are smokers

Large cell lung carcinoma

- typically peripheral
- anaplastic, poorly differentiated tumours with a poor prognosis
- may secrete β-hCG

Next question

Textbooks

High-yield textbook

Extended textbook

Links

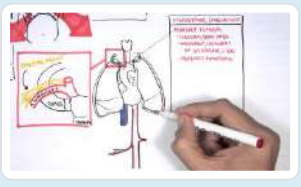
Radiopaedia

4 3

Lung cancer review

Suggest link Report broken link

Media



Lung cancer

Armando Hasudungan - YouTube

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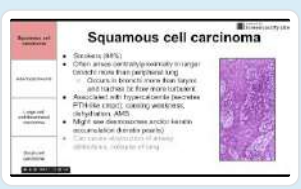
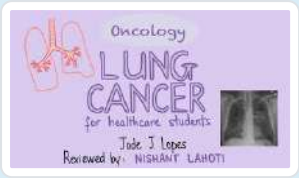


Cancers of the lung

MedLecturesMadeEasy - YouTube 1 0



Lung cancer

MedFlix - YouTube 0 0

Lung Cancer: An Overview

Oncology for Medical Students - YouTube 0 0

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Back to top

A 65-year-old man with metastatic squamous cell lung cancer is admitted to the Acute Medical Unit for the management of hypercalcaemia. He is currently taking slow-release morphine sulphate (MST) 90mg bd to control his pain along with regular naproxen and paracetamol. During his admission he complains of pain in his right arm which is the site of a known skeletal metastasis. What is the most appropriate medication to prescribe to treat his acute pain?

- Oral morphine solution 30mg
- Oral morphine solution 15mg
- Oral morphine solution 10mg
- Add alendronate 70mg weekly
- Tramadol 50mg

Submit answer

Reference ranges

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Oral morphine solution 30mg	63%
Oral morphine solution 15mg	13%
Oral morphine solution 10mg	2%
Add alendronate 70mg weekly	19%
Tramadol 50mg	2%

This patient is describing break-through pain. Whilst bisphosphonates have a role in bone metastases they are not suitable for acute pain. A suitable break-through dose is therefore 1/6th of the total daily morphine dose i.e. 1/6th of 180mg = 30mg.

Discuss (2) | Improve

Next question >

Palliative care prescribing: pain

NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine

solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered
- drowsiness is usually transient - if it does not settle then adjustment of the dose should be considered

SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease
    - oxycodone is preferred to morphine in palliative patients with mild-moderate renal impairment
    - if renal impairment is more severe, alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to strong opioids, bisphosphonates or radiotherapy. The assertion that NSAIDs are particularly effective for metastatic bone pain is not supported by studies. Strong opioids have the lowest number needed to treat for relieving the pain and can provide quick relief, in contrast to radiotherapy and bisphosphonates*. All patients, however, should be considered for referral to a clinical oncologist for consideration of further treatments such as radiotherapy

Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

In addition to strong opioids, bisphosphonates and radiotherapy, denosumab may be used to treat metastatic bone pain.

Opioid side-effects

Usually transient	**Usually persistent**
Nausea Drowsiness	Constipation

Conversion between opioids

From	To	Conversion factor
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

The current BNF gives the following conversion factors for transdermal perparations

- a transdermal fentanyl 12 microgram patch equates to approximately 30 mg oral morphine daily
- a transdermal buprenorphine 10 microgram patch equates to approximately 24 mg oral morphine daily.

From	To	Conversion factor
Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

*BMJ 2015;350:h315 Cancer induced bone pain

**this has previously been stated as 5 but the current version of the BNF states a conversion of 10

***historically a conversion factor of 2 has been used (i.e. oral oxycodone is twice as strong as oral morphine). The current BNF however uses a conversion rate of 1.5

AI + Q 123

Next question >

B I A

Textbooks

High-yield textbook

Extended textbook

Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

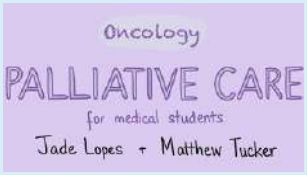
3 3

Prescribing opioids in palliative care

Suggest link

Report broken link

Media



Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube

20 2

Understanding The Causes of Pain and Pain Management

Zero To Finals - YouTube

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Score: **9.3%**

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Back to top

A 77-year-old female is electively admitted for investigation of bilateral lower limb swelling onset over the past 3 years associated with limitation of exercise as a result. Her past medical history includes bilateral pulmonary emboli in 2010 and type 2 diabetes mellitus. On examination, non-pitting bilateral lower limb oedema is noted to the high thighs without abdominal involvement. Her heart sounds are normal with no added sounds, her chest is clear. Her abdomen is soft and non-tender without ascites or superficial swelling. A transthoracic echocardiogram demonstrates normal left ventricular function but was unable to produce good views of the right heart. A CT pulmonary angiogram demonstrates no embolus, a ventilation-perfusion scan demonstrates a low probability of pulmonary emboli. Ultrasound abdomen is unremarkable. The patient undergoes a right heart catheter, demonstrating a mean pulmonary arterial pressure of 14mmHg. What is the likely cause of her lower limb swelling?

- Left heart failure
- Idiopathic pulmonary arterial hypertension
- Right heart failure
- Pelvic malignancy
- Lymphoedema

Submit answer

Reference ranges

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Left heart failure	1%
Idiopathic pulmonary arterial hypertension	7%
Right heart failure	14%
Pelvic malignancy	22%
Lymphoedema	56%

Interpretation of the various investigations this patient has undertaken allows lymphoedema as a diagnosis of exclusion. The patient would have been referred to this standard set of investigations for pulmonary hypertension after clinically presenting as progressive exercise limitation and peripheral oedema, with the primary concern being right heart failure secondary to an increased pressure within the pulmonary vasculature.

Most importantly, the pulmonary arterial pressure is normal on the right heart catheter, ruling idiopathic pulmonary hypertension. Left heart dysfunction is excluded by a normal echocardiogram evaluation of the left ventricular function. CTPA and normal abdominal ultrasound, predominantly investigating the portal circulation, rule out causes of pulmonary hypertension. Lastly, the non-pitting nature of the oedema suggests a non-cardiac cause, making lymphoedema the most likely cause of lower limb swelling.

Lymphoedema

Causes of lymphoedema include:

- primary: inherited
- secondary e.g. surgery, radiation, infection (classically filariasis) or injury resulting in damage to the lymphatic system

123

Next question

Textbooks

High-yield textbook

Extended textbook

Media

Lymphoedema

Osmosis - YouTube 3 0

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Score: **9.3%**

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A 65-year-old man is admitted to the hospital for palliative radiotherapy. He has a squamous cell carcinoma of the tongue that has metastasized to his neck and surrounds the carotid artery. There are no surgical options to treat his disease.

On day 2 of the admission, he experiences a catastrophic bleed from his neck.

What is the most appropriate medication to administer in this circumstance?

- Buscopan
- Chlorpromazine
- Haloperidol
- Midazolam
- Morphine

Submit answer

Reference ranges

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On day 2 of the admission, he experiences a catastrophic bleed from his neck.

What is the most appropriate medication to administer in this circumstance?

Buscopan	4%
Chlorpromazine	3%
Haloperidol	4%
Midazolam	79%
Morphine	10%

In a massive terminal haemorrhage, a large dose of midazolam (10mg) can be given as part of 'crisis management' to relieve distress. Red or green towels or blankets should be available to soak up and mask the colour of blood

Important for me Less important

Midazolam is the correct answer. The patient has experienced a terminal haemorrhage as a consequence of his tumour eroding through the carotid artery. Given the lack of surgical options available to treat his condition, urgent symptom control is warranted to manage this distressing event. Intravenous midazolam is indicated in this horrific situation as a consequence of its anxiolytic and sedative effects, along with the rapidity of its onset.

Haloperidol is incorrect. This can be used to treat agitation in palliative care. However, intravenous midazolam is preferred in this catastrophic situation due to its rapidity of onset.

Morphine is incorrect. This is typically used to treat pain and breathlessness in a palliative care setting, rather than agitation.

Chlorpromazine is incorrect. This can also be used to treat agitation in a palliative care setting. However, midazolam is preferred in terminal haemorrhages.

Buscopan is incorrect. This is used to decrease the burden of secretions in palliative care. It is not used to treat agitation.

Discuss (3) | Improve

Next question ›

Palliative care prescribing: agitation and confusion

Underlying causes of confusion need to be looked for and treated as appropriate, for example hypercalcaemia, infection, urinary retention and medication. If specific treatments fail then the following may be tried:

- first choice: haloperidol
- other options: chlorpromazine, levomepromazine

In the terminal phase of the illness then agitation or restlessness is best treated with midazolam

123

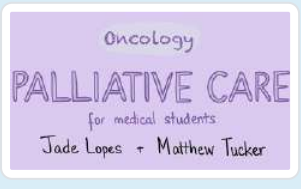
Next question ›

Textbooks

High-yield textbook

Extended textbook

Media



Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube 1 2

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A 64-year-old Nepalese woman who emigrated to the United Kingdom six months prior arrives to her GP. She has known multinodular goitre which has been untreated. However, her daughter who translates for her reports that she has noticed a tight sensation like she is being strangled. This is worse in the mornings and her daughter has noticed that her face does appear puffy. She has no weight loss, fevers or night sweats. She is otherwise well and has never smoked.

On examination, there is a large multinodular goitre that occupies a large part of the neck and measures 15-20cm in width. There is no audible stridor but there are several neck veins visible. You ask her to stretch out her hands up high to observe for a tremor and she starts to complain of the tightness. becoming worse. Her chest sounds are quiet and her chest is clear. There is dull percussion under the top third of the sternum.

TSH	0.07 mU/L (normal range 0.05-5.0)
T4	10 pmol/L (normal range 9-50)
T3	4.0 pmol/L (normal range 3.5-7.8)
D-dimer	0.15 (normal range 0-0.25)
Chest x-ray	Widened mediastinum, no focal lung lesion

What is the underlying cause of these new symptoms?

- Multinodular goitre
- Lymphoma
- Thoracic artery aneurysm
- Lung carcinoma
- Superior vena cava thrombus

Submit answer

Reference ranges

Score: **0%**

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T4	10 pmol/L (normal range 9-50)
T3	4.0 pmol/L (normal range 3.5-7.8)
D-dimer	0.15 (normal range 0-0.25)
Chest x-ray	Widened mediastinum, no focal lung lesion

What is the underlying cause of these new symptoms?

Multinodular goitre	28%
Lymphoma	13%
Thoracic artery aneurysm	4%
Lung carcinoma	4%
Superior vena cava thrombus	50%

Enlarged goitre can be a rare cause of SVC obstruction

Important for me Less important

This presentation is classical for superior vena cava obstruction and the worsening of her symptoms when she lifts her hands up is Pemberton's test which is positive in this case. The next decision is to seek the cause. The obvious cause here is a huge goitre which is recognised as a rare cause of superior cava obstruction. Lung carcinoma is possible but this lady is a non smoker and there is no cough or weight loss. Thoracic artery aneurysm would show a widened mediastinum

but there would often be a history of connective tissue disease or uncontrolled hypertension. Lymphoma causing SVC obstruction would typically have mediastinal lymphadenopathy on chest x-ray. SVC thrombus would be unlikely given that the D-dimer is negative

Discuss (8) | Improve

Next question

Superior vena cava obstruction

Next question

Superior vena cava (SVC) obstruction is an oncological emergency caused by compression of the SVC. It is most commonly associated with lung cancer.

Features

- dyspnoea is the most common symptom
- swelling of the face, neck and arms - conjunctival and periorbital oedema may be seen
- headache: often worse in the mornings
- visual disturbance
- pulseless jugular venous distension

Causes

- common malignancies: small cell lung cancer, lymphoma
- other malignancies: metastatic seminoma, Kaposi's sarcoma, breast cancer
- aortic aneurysm
- mediastinal fibrosis
- goitre
- SVC thrombosis

Management is dependant on the individual patient and malignancy and advice should be taken from the oncology team. Options include:

- endovascular stenting is often the treatment of choice to provide symptom relief
- certain malignancies such as lymphoma, small cell lung cancer may benefit from radical chemotherapy or chemo-radiotherapy rather than stenting
- the evidence base supporting the use of glucocorticoids is weak but they are often given

Textbooks

High-yield textbook

Extended textbook

Media

Superior Vena Cava Syndrome in 3 Minutes

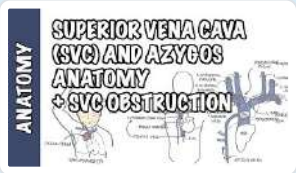
Townsend Teaching - YouTube

2 1

Superior vena cava syndrome

Osmosis - YouTube

2 1



Superior vena cava and the azygos system clinical anatomy - SVC obstruction (oncology emergency)

Armando Hasudungan - YouTube

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Back to top

A 78-year-old gentleman with known metastatic prostate cancer is admitted due to lower back pain that is worse on sitting upright. He denies any sensory changes or weakness but is woken at night and cannot sleep. He takes aspirin, paracetamol and bicalutamide regularly.

On examination, he has normal tone, full power and downgoing plantars in both lower legs. He is exquisitely tender in the midline at L2 and L3.

Bilirubin	34 µmol/l
ALP	450 u/l
ALT	56 u/l
Albumin	32 g/l
Calcium	3.1mmol/l
MRI spine	sclerotic lesions seen in T9, L2 and L3

What medical therapy would offer greatest benefit to him?

- Intravenous fluids
- Denosumab
- Spinal decompressive surgery
- Omeprazole
- Transcutaneous electrical nerve stimulation (TENS)

Submit answer

Reference ranges

Score: **0%**

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Albumin	32 g/l
Calcium	3.1mmol/l
MRI spine	sclerotic lesions seen in T9, L2 and L3

What medical therapy would offer greatest benefit to him?

Intravenous fluids	13%
Denosumab	62%
Spinal decompressive surgery	19%
Omeprazole	0%
Transcutaneous electrical nerve stimulation (TENS)	6%

Denosumab is an unlicensed medication for bony metastasis pain

Important for me Less important

AI

This gentleman has bony pain associated with bony metastases. This is a key question in identifying the problem and how to help him. There is no sign of nerve compression so spinal surgery will not benefit him. He is asymptomatic from his hypercalcaemia so IV fluids would not benefit. Omeprazole will help protect his stomach from ulceration. For bony pain, NSAIDs usually are a good first line. Bisphosphonates and radiotherapy help but are not an answer. Denosumab is

a third line when the above fail. TENS can be useful for all pains but is not evidence based for bony pain.

Discuss (10) | Improve

Next question >

Palliative care prescribing: pain ★

NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered
- drowsiness is usually transient - if it does not settle then adjustment of the dose should be considered

SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease
    - oxycodone is preferred to morphine in palliative patients with mild-moderate renal impairment
    - if renal impairment is more severe, alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to strong opioids, bisphosphonates or radiotherapy. The assertion that NSAIDs are particularly effective for metastatic bone pain is not supported by studies. Strong opioids have the lowest number needed to treat for relieving the pain and can provide quick relief, in contrast to radiotherapy and bisphosphonates*. All patients, however,

should be considered for referral to a clinical oncologist for consideration of further treatments such as radiotherapy

Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

In addition to strong opioids, bisphosphonates and radiotherapy, denosumab may be used to treat metastatic bone pain.

Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

Conversion between opioids

From	To	Conversion factor
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

The current BNF gives the following conversion factors for transdermal perparations

- a transdermal fentanyl 12 microgram patch equates to approximately 30 mg oral morphine daily
- a transdermal buprenorphine 10 microgram patch equates to approximately 24 mg oral morphine daily.

From	To	Conversion factor
Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

*BMJ 2015;350:h315 Cancer induced bone pain

**this has previously been stated as 5 but the current version of the BNF states a conversion of 10

***historically a conversion factor of 2 has been used (i.e. oral oxycodone is twice as strong as oral morphine). The current BNF however uses a conversion rate of 1.5

Next question

Textbooks

High-yield textbook

Extended textbook

Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

3 3

Prescribing opioids in palliative care

Suggest link

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Media

Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube 20 2

Understanding The Causes of Pain and Pain Management

Zero To Finals - YouTube 1 1

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Back to top

You are fast-bleeped to the oncology ward to review a 72-year-old man with a background of metastatic, fungating buccal cancer. During initial MDT, it was deemed inoperable due to carotid artery involvement. He was initially admitted with hypercalcaemia but has deteriorated during his admission and is on the end-of-life pathway.

On your arrival, you note a large amount of blood around the patient with staff using towels and applying pressure to the neck. Nursing staff report that there was a sudden 'pop' and large volume bleeding began at the site of the fungating cancer. They state that bleeding has occurred before but not to this extent.

What is the most appropriate next step in management?

- Adrenaline
- Midazolam
- Morphine
- Terlipressin
- Vascular surgery opinion

Submit answer

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What is the most appropriate next step in management?

Adrenaline	8%
Midazolam	74%
Morphine	5%
Terlipressin	6%
Vascular surgery opinion	7%

In a massive terminal haemorrhage, a large dose of midazolam (10mg) can be given as part of 'crisis management' to relieve distress. Red or green towels or blankets should be available to soak up and mask the colour of blood

Important for me Less important

This is an example of a catastrophic, terminal haemorrhage likely arising from carotid artery involvement. In these circumstances, patients can become very distressed and unfortunately, often there is very little that can be done. To aid in relieving stress it is advised to use red or green towels to help soak up blood as well as obscuring the colour of the blood, as well as giving a large dose of midazolam for relaxation.

Adrenaline can be used in specific circumstances of major haemorrhage but is not used in terminal haemorrhage. Given that the history explains that the patient is on the end of life pathway and that he is not for surgical intervention, adrenaline is not appropriate.

Morphine can be used for pain and breathlessness in palliative care but is not used in terminal haemorrhages.

Terlipressin can be used for major haemorrhage, particularly of gastrointestinal bleeding, however again, this is not appropriate in terminal haemorrhages.

The MDT has already decided that surgical intervention is not appropriate and therefore a vascular surgery opinion at this time would not be appropriate.

Discuss (4) | Improve

Next question

Palliative care prescribing: agitation and confusion

Underlying causes of confusion need to be looked for and treated as appropriate, for example hypercalcaemia, infection, urinary retention and medication. If specific treatments fail then the following may be tried:

- first choice: haloperidol
- other options: chlorpromazine, levomepromazine

In the terminal phase of the illness then agitation or restlessness is best treated with midazolam

123

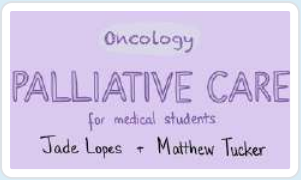
Next question

Textbooks

High-yield textbook

Extended textbook

Media



Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube

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A 60-year-old woman presented to the emergency department with recurrent episodes of severe headache and vomiting over past 3-4 days. She was known to have underlying metastatic breast cancer for which she was receiving palliative chemotherapy. She was also known to have underlying type 2 diabetes mellitus and osteoarthritis of bilateral knee joints.

On examination, her pulse rate was 105/min, respiratory rate was 16/min, blood pressure was 120/80 mmHg. Fundoscopy revealed early papilloedema.

A contrast enhanced CT brain was done which showed a solitary mass of 3 cm in the left cerebral hemisphere.

What is the next appropriate management?

- Start 16 mg of i.v dexamethasone and prophylactic anticonvulsants
- Start 16 mg of dexamethasone and arrange urgent MRI brain
- Refer to neurosurgery for biopsy of the brain lesion
- Refer to radiation oncologist for Whole brain radiotherapy
- Stereotactic radiosurgery

Submit answer

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On examination, her pulse rate was 105/min, respiratory rate was 16/min, blood pressure was 120/80 mmHg. Fundoscopy revealed early papilloedema.

A contrast enhanced CT brain was done which showed a solitary mass of 3 cm in the left cerebral hemisphere.

What is the next appropriate management?

Start 16 mg of i.v dexamethasone and prophylactic anticonvulsants	37%
Start 16 mg of dexamethasone and arrange urgent MRI brain	57%
Refer to neurosurgery for biopsy of the brain lesion	1%
Refer to radiation oncologist for Whole brain radiotherapy	2%
Stereotactic radiosurgery	2%

High dose dexamethasone is the mainstay of immediate management of brain metastasis. For lesions identified as solitary on contrast enhanced CT brain, MRI with gadolinium is indicated to assess the extent of intracranial disease. Patients presenting with seizure activity should be given anticonvulsant therapy. Patients with limited number of lesions(<4) can be considered for more aggressive treatment like neurosurgery or stereotactic radiotherapy but not the immediate step. Biopsy of the lesion is indicated if primary is unknown.Whole brain radiotherapy is indicated for multiple brain metastasis (>4).
Reference: Clinical medicine 2014 Vol 14, No 5: 535-7

Discuss (4) | Improve

Next question >

Breast cancer: management

The management of breast cancer depends on the staging, tumour type and patient background. It may involve any of the following:

- surgery
- radiotherapy
- hormone therapy
- biological therapy
- chemotherapy

Surgery

The vast majority of patients who have breast cancer diagnosed will be offered surgery. An exception may be a very frail, elderly lady with metastatic disease who may be better managed with hormonal therapy.

Prior to surgery, the presence/absence of axillary lymphadenopathy determines management:

- women with no palpable axillary lymphadenopathy at presentation should have a pre-operative axillary ultrasound before their primary surgery
  - if negative then they should have a sentinel node biopsy to assess the nodal burden
- in patients with breast cancer who present with clinically palpable lymphadenopathy, axillary node clearance is indicated at primary surgery
  - this may lead to arm lymphedema and functional arm impairment

Depending on the characteristics of the tumour women either have a wide-local excision or a mastectomy. Around two-thirds of tumours can be removed with a wide-local excision. The table below lists some of the factors determining which operation is offered:

Mastectomy	**Wide Local Excision**
Multifocal tumour	Solitary lesion
Central tumour	Peripheral tumour
Large lesion in small breast	Small lesion in large breast
DCIS > 4cm	DCIS < 4cm

Women should be offered breast reconstruction to achieve a cosmetically suitable result regardless of the type of operation they have. For women who've had a mastectomy this may be done at the initial operation or at a later date.

Radiotherapy

Whole breast radiotherapy is recommended after a woman has had a wide-local excision as this may reduce the risk of recurrence by around two-thirds. For women who've had a mastectomy

radiotherapy is offered for T3-T4 tumours and for those with four or more positive axillary nodes

Hormonal therapy

Adjuvant hormonal therapy is offered if tumours are positive for hormone receptors. For many years this was done using tamoxifen for 5 years after diagnosis. Tamoxifen is still used in pre- and peri-menopausal women. In post-menopausal women, aromatase inhibitors such as anastrozole are used for this purpose*. This is important as aromatisation accounts for the majority of oestrogen production in post-menopausal women and therefore anastrozole is used for ER +ve breast cancer in this group.

Important side effects of tamoxifen include an increased risk of endometrial cancer, venous thromboembolism and menopausal symptoms.

Biological therapy

The most common type of biological therapy used for breast cancer is trastuzumab (Herceptin). It is only useful in the 20-25% of tumours that are HER2 positive.

Trastuzumab cannot be used in patients with a history of heart disorders.

Chemotherapy

Cytotoxic therapy may be used either prior to surgery ('neoadjuvanant' chemotherapy) to downstage a primary lesion or after surgery depending on the stage of the tumour, for example, if there is axillary node disease - FEC-D is used in this situation.

AI + Q 123

Next question >

Textbooks

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Extended textbook

Links

NICE

1 1

Early and locally advanced breast cancer: Diagnosis and treatment

Suggest link Report broken link

Media

Pharmacology - CANCER DRUGS - HORMONAL THERAPY

Speed Pharmacology - YouTube

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Breast cancer

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A 48-year-old woman is currently undergoing various cycles of chemotherapy for breast cancer. She asks the oncology team for advice as, 2-3 days post-chemotherapy, she experiences severe nausea and vomiting that lasts for several days. This is debilitating, despite taking antiemetics during the chemotherapy and afterward.

What is the most appropriate drug to prevent this delayed reaction?

- Dexamethasone
- Levopromazine
- Lorazepam
- Metoclopramide
- Ondansetron

Submit answer

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What is the most appropriate drug to prevent this delayed reaction?

Dexamethasone	42%
Levopromazine	12%
Lorazepam	2%
Metoclopramide	8%
Ondansetron	36%

Dexamethasone is the most useful agent in preventing the delayed phase of chemotherapy-induced emesis

Important for me Less important

Dexamethasone has been shown by numerous trials to be the most effective agent in preventing delayed nausea and vomiting. As opposed to more immediate nausea and vomiting, for which antiemetics are useful, the delayed reaction (between 24 hours and 1-week post-chemotherapy) is not as effectively reduced by antiemetics.

Levopromazine is a 'dirty drug', acting at multiple receptor sites. It is a useful antiemetic, particularly parenterally, but sedates patients quite significantly and is generally reserved for palliative care and intractable symptoms.

Lorazepam, a benzodiazepine, has mild antiemetic properties and is not considered effective at reducing the delayed phase. It is generally used for its anti-anxiolytic properties.

Metoclopramide is a dopamine antagonist and an effective antiemetic. It may be used first-line for immediate nausea and vomiting. However, in the context of the delayed phase, dexamethasone is more useful.

Ondansetron is a serotonin receptor antagonist and another effective antiemetic used for

chemotherapy-induced nausea and vomiting. With regards to the delayed phase, however, dexamethasone is the most effective agent.

Discuss (1) | Improve

Next question

Chemotherapy side-effects: nausea and vomiting

Nausea and vomiting are common side-effects of chemotherapy. Risk factors for the development of symptoms include:

- anxiety
- age less than 50 years old
- concurrent use of opioids
- the type of chemotherapy used

For patients at low-risk of symptoms then drugs such as metoclopramide may be used first-line. For high-risk patients then 5HT3 receptor antagonists such as ondansetron are often effective, especially if combined with dexamethasone

123

Next question

Textbooks

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Media

Physiology of Vomiting - Vomiting reflex

Armando Hasudungan - YouTube 3 0

Pharmacology - Antiemetics

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A 68-year-old man with metastatic prostate cancer is due to go for radiotherapy in an hour. The nurses tell you that he complained of pain during the transfer yesterday. His pain has been otherwise well controlled on a total of 60mg morphine daily. How is it best to manage his pain control for the transfer today?

- Nothing as it is only temporary pain
- An additional dose of 10mg morphine 30 minutes prior to his transfer
- An additional dose of 15mg morphine 1 hour prior to his transfer
- An additional dose of 10mg morphine 1 hour prior to his transfer
- An additional dose of 15mg morphine 30 minutes prior to his transfer

Submit answer

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Nothing as it is only temporary pain	2%
An additional dose of 10mg morphine 30 minutes prior to his transfer	68%
An additional dose of 15mg morphine 1 hour prior to his transfer	3%
An additional dose of 10mg morphine 1 hour prior to his transfer	22%
An additional dose of 15mg morphine 30 minutes prior to his transfer	4%

A breakthrough dose of morphine should be given 30 minutes prior to his transfer as indicated in the BNF. 1 hour is too long prior as it should last him the transfer back and 30 minutes prior is enough for the morphine to have the desired effect. A breakthrough dose should be 1/6th of his total daily dose which in this case is 10mg. Therefore, 15mg is too high a dose for this patient.

Although it is temporary pain, it should still be treated as the patient's comfort and quality of life are important aspects of his care.

Discuss (3) | Improve

Next question

Palliative care prescribing: pain

NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient

preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered
- drowsiness is usually transient - if it does not settle then adjustment of the dose should be considered

SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease
    - oxycodone is preferred to morphine in palliative patients with mild-moderate renal impairment
    - if renal impairment is more severe, alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to strong opioids, bisphosphonates or radiotherapy. The assertion that NSAIDs are particularly effective for metastatic bone pain is not supported by studies. Strong opioids have the lowest number needed to treat for relieving the pain and can provide quick relief, in contrast to radiotherapy and bisphosphonates*. All patients, however, should be considered for referral to a clinical oncologist for consideration of further treatments such as radiotherapy

Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

In addition to strong opioids, bisphosphonates and radiotherapy, denosumab may be used to treat metastatic bone pain.

Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

Conversion between opioids

From	To	Conversion factor
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Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

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*BMJ 2015;350:h315 Cancer induced bone pain

**this has previously been stated as 5 but the current version of the BNF states a conversion of 10

***historically a conversion factor of 2 has been used (i.e. oral oxycodone is twice as strong as oral morphine). The current BNF however uses a conversion rate of 1.5

AI + Q 123

Next question ›

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Textbooks

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Links

NICE

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2012 Opioids in palliative care guidelines

BNF

3 3

Prescribing opioids in palliative care

Suggest link

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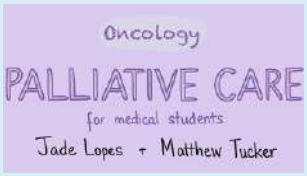
Media



Complete Guide to Palliative Care for Medical Students

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Understanding The Causes of Pain and Pain Management

Zero To Finals - YouTube

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Score: **9.3%**

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A 72-year-old man presents to the emergency department with shortness of breath. He describes his breathlessness has progressively become worse over the last two weeks and is especially troublesome when leaning forward. His wife has commented that his appearance has changed too, with his face becoming more swollen and different in colour. He has a past medical history of right-sided heart failure, myocardial infarction, type two diabetes, COPD and small cell lung cancer diagnosed three months ago. He is an ex-smoker of 20 pack-years and drinks moderate amounts of alcohol.

On examination, he appears settled at rest. His face is swollen and slightly purple. His neck veins are distended and his JVP is markedly elevated to 4cm. Auscultation reveals bibasal crepitations. There is pitting oedema at the ankles. A chest X-ray demonstrates a widened mediastinum. What investigation is most appropriate to establish the diagnosis?

- ECG
- Trans-thoracic echocardiogram
- Trans-oesophageal echocardiogram
- Bronchoscopy
- CT chest

Submit answer

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ECG	1%
Trans-thoracic echocardiogram	11%
Trans-oesophageal echocardiogram	7%
Bronchoscopy	3%
CT chest	78%

The correct answer is CT chest as the patient has a clinical history consistent with obstruction of the superior vena cava (SVC). There are several symptoms and signs consistent with SVC obstruction, including breathlessness worse, leaning forward, distended neck veins and a swollen face. This, in combination with known lung cancer, suggests progression of the primary malignancy or lymph nodes compressing the SVC. Whilst some of the finds could be suggestive of acute pulmonary oedema, the chest X-ray is consistent with SVC obstruction. As a cardiac cause is unlikely, an echocardiogram or ECG is unlikely to be diagnostic. A bronchoscopy is a possible approach for obtaining a biopsy if an SVC obstruction is diagnosed and the source of the obstruction is unclear, but as this patient is known to have lung cancer this is not going to be helpful for this patient.

Source:

Drews, Reed E., and Dmitry J. Rabkin. 'Malignancy-related Superior Vena Cava Syndrome.' UpToDate. N.p., 2 Mar. 2016.

Superior vena cava obstruction

Superior vena cava (SVC) obstruction is an oncological emergency caused by compression of the SVC. It is most commonly associated with lung cancer.

Features

- dyspnoea is the most common symptom
- swelling of the face, neck and arms - conjunctival and periorbital oedema may be seen
- headache: often worse in the mornings
- visual disturbance
- pulseless jugular venous distension

Causes

- common malignancies: small cell lung cancer, lymphoma
- other malignancies: metastatic seminoma, Kaposi's sarcoma, breast cancer
- aortic aneurysm
- mediastinal fibrosis
- goitre
- SVC thrombosis

Management is dependant on the individual patient and malignancy and advice should be taken from the oncology team. Options include:

- endovascular stenting is often the treatment of choice to provide symptom relief
- certain malignancies such as lymphoma, small cell lung cancer may benefit from radical chemotherapy or chemo-radiotherapy rather than stenting
- the evidence base supporting the use of glucocorticoids is weak but they are often given

Textbooks

High-yield textbook

Extended textbook

Media

Superior Vena Cava Syndrome in 3 Minutes

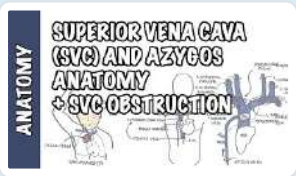
Townsend Teaching - YouTube

2 1

Superior vena cava syndrome

Osmosis - YouTube

2 1



Superior vena cava and the azygos system clinical anatomy - SVC obstruction (oncology emergency)

Armando Hasudungan - YouTube

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Report broken media

Score: **9.3%**

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Back to top

A 40-year-old man is seen in the Emergency Department with breathlessness.

He was diagnosed with non-Hodgkin lymphoma 6 months ago and has been receiving chemotherapy. He is awaiting an appointment in haematology outpatients to assess his response to chemotherapy.

He describes becoming more breathless over the last week and feeling that his arms and face are puffy. He has had no chest pain, cough or fevers.

On examination his oxygen saturations are 92% on air and his heart rare is 112 beats per minute. His chest is clear and he is unable to lay flat for his abdomen to be examined due to is breathlessness. His face appears flushed and he has oedema of the arms and hands. His neck veins appear engorged.

Chest x-ray shows a widened mediastinum with extensive lymphadenopathy.

A CT scan of the thorax confirms superior vena cava obstruction (SVCO). The scan is reviewed by the haematology team who explain to him that his lymphoma has progressed despite chemotherapy.

He is started on steroids and a proton pump inhibitor.

What is the next step in the management of this gentleman's SVCO?

- Chemotherapy
- Observation
- Radiotherapy
- Stent insertion
- Surgery

Submit answer

Reference ranges

Score: **0%**

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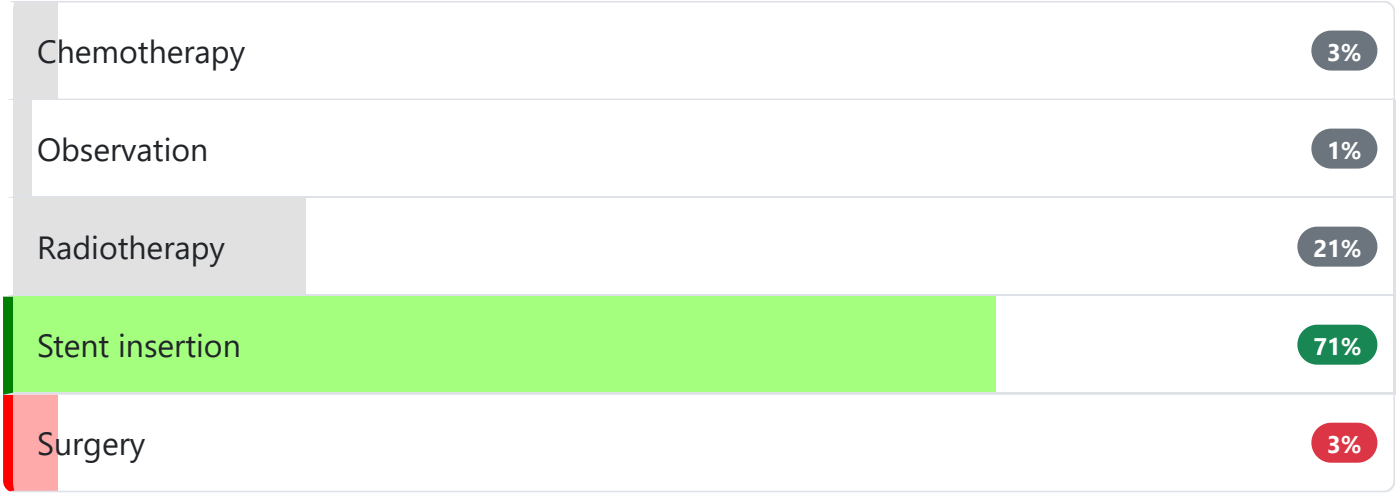

SVCO is an oncological emergency and is most common in lung cancer and lymphomas. The immediate management is steroids with proton pump inhibitor cover for gastric protection.

Further options include stent insertion, radiotherapy and chemotherapy.

This gentleman is unable to lay flat so would not be able to tolerate radiotherapy. Radiotherapy

also has the disadvantage of causing increased swelling acutely before it causes long term shrinkage.

Lymphomas are highly chemotherapy responsive tumours and this gentleman has only had first-line chemotherapy, therefore second-line chemotherapy should be planned in order to shrink his mediastinal disease.

Stent insertion is the most immediate management for relieving SVCO until chemotherapy can take effect. The patient's haemoglobin, platelets and clotting must be checked and optimised. In patients with end-stage disease, stents can still become blocked.

Surgery is not generally part of the management for SVCO.

Reference:
London Cancer Alliance. Acute Oncology Clinical Guidelines. 2013.

Discuss (3) | Improve

Next question >

Superior vena cava obstruction ★

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123

Next question

Textbooks

High-yield textbook

Extended textbook

Media

Superior Vena Cava Syndrome in 3 Minutes

Townsend Teaching - YouTube

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Superior vena cava syndrome

Osmosis - YouTube

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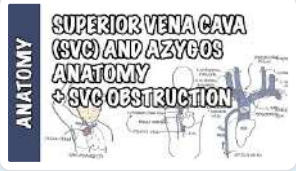

Superior vena cava and the azygos system clinical anatomy - SVC obstruction (oncology emergency)

Armando Hasudungan - YouTube

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Score: **9.3%**

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Back to top

A 71-year-old woman is referred by her GP to the rapid access chest clinic with progressive shortness of breath and reduced exercise tolerance over 3 months and a chronic productive cough. When asked about her past medical history she states that she has had some pain for the past month or so in her left shoulder, which has been present at a constant level. She has been taking paracetamol and codeine for the pain which helps slightly. Otherwise, the patient has moderate COPD, for which she taken ipratropium bromide and salmeterol and mechanical back pain. She has a 15 year pack-history and drinks 1-2 units of alcohol per day.

Examination reveals some wasting of the hypothenar eminence of the left hand, although the chest sounds clear bilaterally with no added sounds. Heart sounds 1 and 2 are present with no murmurs.

What would be the most useful investigation following a chest x-ray?

- Electromyogram studies
- Computed tomography of the thorax
- Bronchoscopy
- Myeloma screen
- Sputum microscopy, culture and sensitivity

Submit answer

Reference ranges

Score: **0%**

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What would be the most useful investigation following a chest x-ray?

Electromyogram studies	6%
Computed tomography of the thorax	81%
Bronchoscopy	5%
Myeloma screen	6%
Sputum microscopy, culture and sensitivity	2%

The most likely diagnosis in this case is lung malignancy, in particular a Pancoast tumour, given this patient's wasting of the hypothenar eminence, shortness of breath and cough. The most useful investigation is a CT of the thorax - bronchoscopy is not as useful as the cancer is often too peripheral.

Discuss (3) | Improve

Next question

Lung cancer: non-small cell

There are three main subtypes of non-small cell lung cancer:

Squamous cell cancer

- typically central
- associated with parathyroid hormone-related protein (PTHrP) secretion → hypercalcaemia
- strongly associated with finger clubbing
- cavitating lesions are more common than other types
- hypertrophic pulmonary osteoarthropathy (HPOA)

Adenocarcinoma

- typically peripheral
- most common type of lung cancer in non-smokers, although the majority of patients who develop lung adenocarcinoma are smokers

Large cell lung carcinoma

- typically peripheral
- anaplastic, poorly differentiated tumours with a poor prognosis
- may secrete β-hCG

Next question

Textbooks

High-yield textbook

Extended textbook

Links

Radiopaedia

4 3

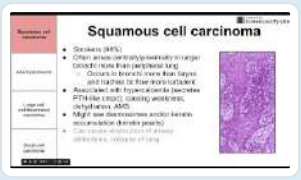
Lung cancer review

Suggest link Report broken link

Media

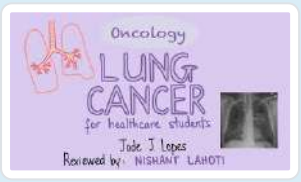
Lung cancer

Armando Hasudungan - YouTube 1 0



Cancers of the lung

MedLecturesMadeEasy - YouTube 1 0



Lung cancer

MedFlix - YouTube 0 0

Lung Cancer: An Overview

Oncology for Medical Students - YouTube 0 0

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Score: **9.3%**

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You are asked to review a 67-year-old gentleman who was admitted to the medical emergency unit with pneumonia. He had been diagnosed with terminal small cell cancer of the lung which had extensively metastasised to his liver, thoracic vertebrae and femur bones. His past medical history was comprised of ischaemic heart disease, hypertension, hypercholesterolaemia and COPD.

His main complaint was of progressively worsening pain in his spine and legs. This was particularly bothersome at night; a trial of bisphosphonate therapy and radiotherapy did not provide any symptomatic relief. He was commenced initially on oral morphine sulphate solution which was converted to morphine sulphate tablets (MST); he had been on 60mg BD but this was titrated by the palliative care community nurse to 70mg BD a couple of days prior to admission with excellent analgesic effect. He was also using Oramorph solution 10mg on average 5-6 times a day for breakthrough pain.

He had been accordingly treated with intravenous antibiotics whilst on the ward making a full recovery. Prior to discharge, he was very keen on commencing transdermal treatment so as to minimise the number of oral medications taken.

What is the most appropriate starting dose to commence, with a view to completely discontinuing all oral opiate medication?

- Commence Fentanyl 12 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain
- Commence Fentanyl 25 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain
- Commence Fentanyl 50 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain
- Commence Fentanyl 75 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain
- Commence Fentanyl 100 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain

Submit answer

Reference ranges

Score: **0%**

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Commence Fentanyl 12 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain	9%
Commence Fentanyl 25 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain	17%
Commence Fentanyl 50 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain	30%
Commence Fentanyl 75 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain	30%
Commence Fentanyl 100 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain	13%

This gentleman was on a rather complicated opiate analgesia regimen and the key to this question is calculate the total daily dose of morphine salt, to then convert it to the appropriate amount of fentanyl.

His total morphine salt intake was thus:

MST 70mg BD = 140mg of morphine
Oramorph 10mg PRN = 50-60mg of morphine

Total = 190-200mg daily morphine salt intake

The BNF states that a fentanyl 75 patch is equivalent to 180mg daily intake of morphine salt whilst a fentanyl 100patch is equivalent to 240mg daily morphine salt intake. So as to avoid opiate toxicity the correct answer is thus to commence a fentanyl 75 patch and to supplement this with PRN Oramorph solution.

Discuss (6) | Improve

Next question >

Palliative care prescribing: pain

NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered
- drowsiness is usually transient - if it does not settle then adjustment of the dose should be considered

SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease

    - oxycodone is preferred to morphine in palliative patients with mild-moderate renal impairment
    - if renal impairment is more severe, alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to strong opioids, bisphosphonates or radiotherapy. The assertion that NSAIDs are particularly effective for metastatic bone pain is not supported by studies. Strong opioids have the lowest number needed to treat for relieving the pain and can provide quick relief, in contrast to radiotherapy and bisphosphonates*. All patients, however, should be considered for referral to a clinical oncologist for consideration of further treatments such as radiotherapy

Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

In addition to strong opioids, bisphosphonates and radiotherapy, denosumab may be used to treat metastatic bone pain.

Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

Conversion between opioids

From	To	Conversion factor
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

The current BNF gives the following conversion factors for transdermal perparations

- a transdermal fentanyl 12 microgram patch equates to approximately 30 mg oral morphine daily
- a transdermal buprenorphine 10 microgram patch equates to approximately 24 mg oral morphine daily.

From	To	Conversion factor
Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

*BMJ 2015;350:h315 Cancer induced bone pain

**this has previously been stated as 5 but the current version of the BNF states a conversion of 10

***historically a conversion factor of 2 has been used (i.e. oral oxycodone is twice as strong as oral morphine). The current BNF however uses a conversion rate of 1.5

Next question

Textbooks

High-yield textbook

Extended textbook

Links

NICE

3 1

2012 Opioids in palliative care guidelines

BNF

3 3

Prescribing opioids in palliative care

Suggest link Report broken link

Media

Complete Guide to Palliative Care for Medical Students

MedFlix - YouTube 20 2

Understanding The Causes of Pain and Pain Management

Zero To Finals - YouTube 1 1

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Score: **9.3%**

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A 68-year-old man presents with a five-week history of lower back pain that is worse with coughing. He has noticed that he has been requiring more painkillers to the point where he is struggling to manage, especially at night. The pain is worse when straining to pass stool. He lost three kg over the last four months as well. He has a past medical history of COPD, hypertension, type two diabetes mellitus, and hypercholesterolemia. He has been admitted three times in the last year for exacerbations of COPD requiring the recurrent use of oral prednisolone. His regular medications include Symbicort, tiotropium, atorvastatin, metformin, paracetamol, codeine and Movicol. He is an ex-smoker with a 50 pack-year history and recently opted for early retirement from his job as an accountant as he was struggling with tiredness. On examination, he appears tired and his clothes appear loose fitting. Examination of his chest is unremarkable, but there is a 1cm swelling above his left clavicle. His abdomen is soft, there is no tenderness over his spine, and a neurological examination is unremarkable.

Observations:

Saturations	95%
Respiratory rate	15/min
Blood pressure	148/87mmHg
Heart rate	74/min
Temperature	37.4°C

Blood tests:

Hb	128 g/l
MCV	72 fl
Platelets	327 * 10^9/l
WBC	12.4 * 10^9/l
Na^+	136 mmol/l
K^+	4.2 mmol/l
Urea	4.1 mmol/l
Creatinine	77 µmol/l

What is the most likely diagnosis that explains his symptoms?

- Osteoporotic vertebral collapse
- Spinal cord metastasis

- Myeloma
- Degenerative changes
- Discitis

Submit answer

Reference ranges

Score: **0%**

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Creatinine	77 µmol/l

What is the most likely diagnosis that explains his symptoms?

Osteoporotic vertebral collapse	8%
Spinal cord metastasis	80%

Myeloma	7%
Degenerative changes	1%
Discitis	4%

The answer is spinal cord metastasis. This question highlights multiple subtle red flags in a history with back pain. He is over >55 and describes nocturnal and progressive pain worse with coughing and straining in the context of immunosuppression from repeated steroid use, weight loss, and increasing fatigue. Due to the high suspicion, the most diagnostic imaging investigation would be a whole spine MRI, which would differentiate between the above diagnoses. Osteoporotic fracture is suggested by the use of steroids but overall does not fit with the progressive nature and microcytic anaemia, nor do degenerative changes. There are very few symptoms to suggest infection such as fever and night sweats, but discitis cannot be fully excluded without imaging. Myeloma is a possible diagnosis, but so far there are no specific factors to suggest it, such as lytic bone lesions or deteriorating renal function.

Discuss (6) Improve

Next question

Spinal metastases

Patients may present with spinal metastases before developing metastatic spinal cord compression. It is, therefore, important to detect these patients early before any neurological compromise develops.

Symptoms and findings

- Unrelenting lumbar back pain
- Any thoracic or cervical back pain
- Worse with sneezing, coughing or straining
- Nocturnal
- Associated with tenderness

If any neurological features are present then spinal cord compression must be suspected and acted on promptly. Without neurological features, a whole spine MRI should be completed within one week. The whole spine should be imaged as patients commonly present with multi-level disease.

Sources:
Al-Qurainy, Rasha, and Emily Collis. 'Metastatic Spinal Cord Compression: Diagnosis and Management.' Bmj (2016): I2539.

Metastatic Spinal Cord Compression in Adults: Risk Assessment, Diagnosis and Management Clinical Guideline [CG75]. National Institute of Clinical Excellence. N.p., Nov. 2008.

Next question

Textbooks

High-yield textbook

Extended textbook

Score: **9.3%**

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A 56-year-old male with non-hodgkin's lymphoma is on his third cycle of R-CHOP chemotherapy. He has struggled previous times with nausea but is two days following the most recent cycle and attended hospital due to intractable vomiting.

He is vomiting 20+ times a day with green to clear fluid. He does not feel hungry and struggles to swallow water. He is not having diarrhoea. He takes regular indapamide and as required ondansetron and this has not helped him despite the oncologist suggesting he double his dose of ondansetron.

On examination, he looks pale and has dry mucosa. He is alert, has a clear chest and soft abdomen but begins to retch on sitting forward. He last passed urine 6 hours ago and his observations show a heart rate of 115 beats per minute and blood pressure 90/65mmHg. He is started on intravenous fluids by the emergency department.

Na^+	135 mmol/l
K^+	3.5 mmol/l
Urea	6.5 mmol/l
Creatinine	98 µmol/l

What medical intervention would offer greatest benefit?

- Cyclizine
- Potassium salt replacement
- Elective terminal ileostomy
- Dexamethasone
- Delay next course of chemotherapy

Submit answer

Reference ranges

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Na^+	135 mmol/l
K^+	3.5 mmol/l
Urea	6.5 mmol/l
Creatinine	98 µmol/l

What medical intervention would offer greatest benefit?

Cyclizine	17%
Potassium salt replacement	2%
Elective terminal ileostomy	1%
Dexamethasone	**76%**
Delay next course of chemotherapy	5%

Dexamethasone with ondansetron is effective in refractory chemotherapy-induced vomiting

Important for me Less important

This gentleman has refractory vomiting despite ondansetron. He need assistance to ensure he can maintain fluids. Cyclizine is an antiemetic but bind histamine receptors so is most useful in

labyrinthitis and motion sickness. Potassium salt replacement will probably make him vomit more but does replace his lost salts. Delaying the course of chemotherapy would be an option if nothing else could be offered. Surgery is not the way forward here. Dexamethasone is proven as an effective second line antiemetic in chemotherapy related nausea and vomiting. it is often given in lymphoma to prevent tumour lysis syndrome.

Discuss (6) | Improve

Next question ›

Chemotherapy side-effects: nausea and vomiting

Nausea and vomiting are common side-effects of chemotherapy. Risk factors for the development of symptoms include:

- anxiety
- age less than 50 years old
- concurrent use of opioids
- the type of chemotherapy used

For patients at low-risk of symptoms then drugs such as metoclopramide may be used first-line. For high-risk patients then 5HT3 receptor antagonists such as ondansetron are often effective, especially if combined with dexamethasone

AI + Q 123

Next question ›

B I A T↕

Textbooks

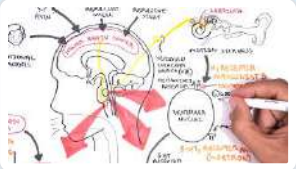
High-yield textbook

Extended textbook

Media

Physiology of Vomiting - Vomiting reflex

Armando Hasudungan - YouTube 3 0



Pharmacology - Antiemetics

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A 38-year-old man presents with increasing shortness of breath and ankle swelling. He reports he is more short of breath, especially on exertion, which is not being relieved by the use of his salbutamol inhaler. He has also noticed his ankles are swollen by the end of the day.

His past medical history includes asthma, which is usually well controlled, and lymphoma, which was treated with chemotherapy several years ago. His only medications are his beclometasone and salbutamol inhalers. The results of his blood tests are shown below:

Hb	140 g/L	(135-180)
Platelets	359 * 10^9/L	(150 - 400)
WBC	7.2 * 10^9/L	(4.0 - 11.0)
Na^+	137 mmol/L	(135 - 145)
K^+	4.3 mmol/L	(3.5 - 5.0)
Urea	5.9 mmol/L	(2.0 - 7.0)
Creatinine	119 µmol/L	(55 - 120)

His ECG showed sinus rhythm with left axis deviation. An echocardiogram was done which showed dilation of all four chambers of the heart and a left ventricular ejection fraction of 40%.

Which drug can be attributed to causing this man's presentation?

- Cyclophosphamide
- Vincristine
- Doxorubicin
- Docetaxel
- Bleomycin

Submit answer

Reference ranges

Score: **0%**

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Urea	5.9 mmol/L	(2.0 - 7.0)
Creatinine	119 µmol/L	(55 - 120)

His ECG showed sinus rhythm with left axis deviation. An echocardiogram was done which showed dilation of all four chambers of the heart and a left ventricular ejection fraction of 40%.

Which drug can be attributed to causing this man's presentation?

- Cyclophosphamide 1%
- Vincristine 2%
- Doxorubicin 88%
- Docetaxel 4%
- Bleomycin 5%

Anthracyclines (e.g. doxorubicin) may cause cardiomyopathy

Important for me Less important

This man is presenting with features of heart failure and the echocardiogram results would be in keeping with a diagnosis of dilated cardiomyopathy. Doxorubicin (an anthracycline) is used in the treatment of lymphoma and is known to be cardiotoxic.

Cyclophosphamide can also be used to treat lymphoma and other haematological conditions such as leukaemia. A well-known side effect is haemorrhagic cystitis.

Vincristine can be used with doxorubicin to treat lymphoma and is associated with peripheral neuropathy.

Docetaxel is often used in the management of breast and lung cancers and can cause neutropenia.

Bleomycin can be used as part of lymphoma management and is associated with the development of pulmonary fibrosis.

Discuss (2) | Improve

Next question >

Cytotoxic agents

The tables below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents.

Alkylating agents

Cytotoxic	Mechanism of action	Adverse effects
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma

Cytotoxic antibiotics

Cytotoxic	Mechanism of action	Adverse effects
Bleomycin	Degrades preformed DNA	Lung fibrosis
Anthracyclines (e.g doxorubicin)	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy

Antimetabolites

Cytotoxic	Mechanism of action	Adverse effects
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis, lung fibrosis
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis by blocking thymidylate synthase (works during S phase)	Myelosuppression, mucositis, dermatitis
6-mercaptopurine	Purine analogue that is activated by HGPRTase, decreasing purine synthesis	Myelosuppression
Cytarabine	Pyrimidine antagonist. Interferes with DNA synthesis specifically at the S-phase of the cell cycle and inhibits DNA polymerase	Myelosuppression, ataxia

Acts on microtubules

Cytotoxic	Mechanism of action	Adverse effects
Vincristine, vinblastine	Inhibits formation of microtubules	Vincristine: Peripheral neuropathy (reversible) , paralytic ileus Vinblastine: myelosuppression
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Topoisomerase Inhibitors

Cytotoxic	Mechanism of action	Adverse effects
Irinotecan	Inhibits topoisomerase I which prevents relaxation of supercoiled DNA	Myelosuppression

Other cytotoxic drugs

Cytotoxic	Mechanism of action	Adverse effects
Cisplatin	Causes cross-linking in DNA	Nephrotoxicity (the primary dose-limiting side effect), Ototoxicity, peripheral neuropathy, hypomagnesaemia
Hydroxyurea (hydroxycarbamide)	Inhibits ribonucleotide reductase, decreasing DNA synthesis	Myelosuppression

123

Next question

Textbooks

High-yield textbook

Extended textbook

Links

Toxicity Bear's very own website

339

17

Toxicity Bear

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Media

Pharmacology - Chemotherapy agents

Armando Hasudungan - YouTube 4 0

Cancer Pharmacology

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Microtubule inhibitors

Osmosis - YouTube 3 0

Cancer Drugs - Learn with Visual Mnemonics!

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Back to top

You are reviewing a 65-year-old man who has recently started treatment for urological cancer with Nivolumab (Opdivo) a type of checkpoint inhibitor.

He has been having treatment for 1 month and has had no side effects so far. He would like to know what to expect from this treatment.

What is the most common side effect this patient is likely to experience?

- Dry itchy skin and rashes
- Depression and anxiety
- Dry cough
- Retinal damage
- Skin discolouration

Submit answer

Reference ranges

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You are reviewing a 65-year-old man who has recently started treatment for urological cancer with Nivolumab (Opdivo) a type of checkpoint inhibitor.

He has been having treatment for 1 month and has had no side effects so far. He would like to know what to expect from this treatment.

What is the most common side effect this patient is likely to experience?

Dry itchy skin and rashes	57%
Depression and anxiety	14%
Dry cough	8%
Retinal damage	9%
Skin discolouration	11%

The most common side effect of immune checkpoint inhibitors is dry itchy skin and rashes

Important for me Less important

Immune checkpoint inhibitors are a type of immunotherapy that are increasingly being used to treat certain types of cancer, as an alternative to cytotoxic chemotherapy. They are currently only used to treat solid tumours. They work by enhancing the bodies own T-cell population to destroy the cancer cells.

Their side effect profile reflects their mechanism of action and are, therefore, inflammatory and autoimmune in nature. They include:

- Dry, itchy skin and rashes (most commonly)
- Nausea and vomiting
- Decreased appetite
- Diarrhoea
- Tiredness and fatigue
- Shortness of breath and a dry cough.

Therefore, option one is the only correct answer.

Immune checkpoint inhibitors

Immune checkpoint inhibitors are a type of immunotherapy that are increasingly being used to treat certain types of cancer, as an alternative to cytotoxic chemotherapy. In contrast to therapies such as chemotherapy and tumour-targeted drugs that directly affect the growth and proliferation of tumour cells, these targeted treatments harness the body's natural anti-cancer immune response. They boost its ability to attack and destroy the cancer cells.

T-cells are an important part of our immune system which help destroy cancer cells. Some cancer cells make high levels of proteins that turn T-cells off. Checkpoint inhibitors block this process and reactivate and increase the body's own T-cell population, enhancing the immune systems own ability to recognise and fight cancer cells.

Types:

- Ipilimumab (Yervoy) is a checkpoint inhibitor that blocks CTLA-4 (cytotoxic T lymphocyte-associated protein 4). It is a treatment for advanced melanoma.
- Nivolumab (Opdivo) and pembrolizumab (Keytruda) blocks PD-1 (programmed cell death protein 1). These are treatments for melanoma, Hodgkin's lymphoma, non-small cell lung cancer and urological cancers.
- Atezolizumab, Avelumab and Durvalumab block PD-L1 and is used to treat lung cancer and urothelial cancer. It is also undergoing trials as a treatment for breast cancer.

The proteins CTLA-4 and PD-1 are found on T-cells and PD-L1 are found on cancer cells.

Administration

All CTLA-4 inhibitors and PD-1/PD-L1 inhibitors currently available are monoclonal antibodies (laboratory-produced molecules engineered to serve as substitute antibodies that each bind to a specific protein). They are all administered by injection/intravenous infusion. Mostly, they are given as a single-agent treatment but sometimes, they can be combined with chemotherapy or each other. For example, ipilimumab and nivolumab can be used in combination.

Side effects

This mechanism of action of these drugs can result in side effects termed 'Immune-related adverse events' that are inflammatory and autoimmune in nature. This is because all immune cells are

boosted by these drugs, not just the ones that target cancer. The over-active T-cells can produce side effects such as:

- Dry, itchy skin and rashes (most commonly)
- Nausea and vomiting
- Decreased appetite
- Diarrhoea
- Tiredness and fatigue
- Shortness of breath and a dry cough.

Management of such side effects reflects the inflammatory nature, often involving corticosteroids.

It is important to monitor liver, kidney and thyroid function as these drugs can affect these organs.

The future

The early success of immune checkpoint inhibitors in solid tumours has generated a tremendous interest in further developing and exploring these strategies across the oncology disease spectrum. Their ongoing testing in clinical trials creates new hope for patients affected by other types of disease.

Next question

Textbooks

High-yield textbook

Extended textbook

Score: **9.3%**

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A 54-year-old male presents to the emergency department with sudden onset palpitations and shortness of breath which began whilst he was watching television a few hours previously. He describes an odd fluttering sensation in his chest with mild dyspnoea but no chest pain. He denies having experienced this before. On systems review, he also complains of severe muscle cramps and a slight tremor in his hands over the last few days. His past medical history includes hypertension and gout for which he takes amlodipine and allopurinol. He denies any history of exertional dyspnoea but does occasionally get central chest pain on exertion for which he has not sought help. He has recently been diagnosed with small cell lung cancer and underwent his first round of chemotherapy last week; although he is unsure which drugs are being used. He used to smoke a pipe until his recent diagnosis of cancer and drinks a few measures of whisky most evenings.

On examination, his respiratory rate is 22 breaths/min and his oxygen saturations are 96% breathing two litres of oxygen. His heart rate is irregularly irregular and approximately 130 beats/min, his blood pressure is 152/78 mmHg. An ECG shows atrial fibrillation with no ischaemic changes.

What is the most likely cause for his new atrial fibrillation?

- Ischaemic heart disease
- Chemotherapy induced hypokalaemia
- Chemotherapy induced hypomagnesaemia
- Chemotherapy induced cardiomyopathy
- Alcohol

Submit answer

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Score: **0%**

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What is the most likely cause for his new atrial fibrillation?

Ischaemic heart disease	2%
Chemotherapy induced hypokalaemia	14%
Chemotherapy induced hypomagnesaemia	53%
Chemotherapy induced cardiomyopathy	25%
Alcohol	6%

The most common chemotherapy regime for small cell lung cancer is etoposide and cisplatin. A common side effect of cisplatin is hypomagnesaemia which can result in muscle cramps, tremor, cardiac arrhythmias, confusion amongst other features. This gentleman appears to have angina and may well have some level of ischaemic heart disease in the background which would increase his risk of atrial fibrillation. However, it seems logical given the strong temporal relationship between the chemotherapy and the other symptoms of hypomagnesaemia that this is the cause.

Cytotoxic agents ★

The tables below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents.

Alkylating agents

Cytotoxic	Mechanism of action	Adverse effects
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma

Cytotoxic antibiotics

Cytotoxic	Mechanism of action	Adverse effects
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Anthracyclines (e.g doxorubicin)	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy

Antimetabolites

Cytotoxic	Mechanism of action	Adverse effects
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis, lung fibrosis
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6-mercaptopurine	Purine analogue that is activated by HGPRTase, decreasing purine synthesis	Myelosuppression
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Acts on microtubules

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Topoisomerase Inhibitors

Cytotoxic	Mechanism of action	Adverse effects
Irinotecan	Inhibits topoisomerase I which prevents relaxation of supercoiled DNA	Myelosuppression

Other cytotoxic drugs

Cytotoxic	Mechanism of action	Adverse effects
Cisplatin	Causes cross-linking in DNA	Nephrotoxicity (the primary dose-limiting side effect), Ototoxicity, peripheral neuropathy, hypomagnesaemia
Hydroxyurea (hydroxycarbamide)	Inhibits ribonucleotide reductase, decreasing DNA synthesis	Myelosuppression

AI + Q 123

Next question >

B I A T↕

Textbooks

High-yield textbook

Extended textbook

Links

Toxicity Bear's very own website

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Toxicity Bear

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Media

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A 63-year-old man is diagnosed with colorectal cancer. Following successful resection he starts adjuvant capecitabine but after six doses develops severe diarrhoea, weakness and desquamation of the hands, feet and face. On admission, he is pancytopenic and has electrolyte abnormalities requiring IV replacement. His initial blood tests are shown bellow.

Na^+	140 mmol/l
K^+	3.6 mmol/l
Urea	9.2 mmol/l
Creatinine	125 µmol/l
Hb	75 g/l
Platelets	35 * 10^9/l
WBC	0.4 * 10^9/l
Neutrophils	0.03 * 10^9/l
Adjusted Ca^{2+}	1.5 mmol/l
Mg^{2+}	0.32 mmol/l
Glucose	4.0 mmol/l

What is the most likely cause?

- DPD (dihydropyrimidine dehydrogenase) deficiency
- Infective gastroenteritis
- Cancer recurrence
- Pityriasis alba
- Neutropenic sepsis

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Reference ranges

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A 63-year-old man is diagnosed with colorectal cancer. Following successful resection he starts adjuvant capecitabine but after six doses develops severe diarrhoea, weakness and desquamation of the hands, feet and face. On admission, he is pancytopenic and has electrolyte abnormalities requiring IV replacement. His initial blood tests are shown bellow.

Na^+	140 mmol/l
K^+	3.6 mmol/l
Urea	9.2 mmol/l
Creatinine	125 µmol/l
Hb	75 g/l
Platelets	35 * 10^9/l
WBC	0.4 * 10^9/l
Neutrophils	0.03 * 10^9/l
Adjusted Ca^{2+}	1.5 mmol/l
Mg^{2+}	0.32 mmol/l
Glucose	4.0 mmol/l

What is the most likely cause?

- DPD (dihydropyrimidine dehydrogenase) deficiency — 63%
- Infective gastroenteritis — 3%
- Cancer recurrence — 1%
- Pityriasis alba — 2%
- Neutropenic sepsis — 31%

Capecitabine is the oral analog of 5-fluorouracil, a chemotherapeutic agent which is broken down, predominantly, by dihydropyrimidine dehydrogenase (DPD). Deficiency is autosomal recessive and will lead to a toxin buildup which in homozygous patients is usually fatal. The severe toxicity experienced by this patient are likely due to a heterozygous DPD deficiency.

Cytotoxic agents

The tables below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents.

Alkylating agents

Cytotoxic	Mechanism of action	Adverse effects
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma

Cytotoxic antibiotics

Cytotoxic	Mechanism of action	Adverse effects
Bleomycin	Degrades preformed DNA	Lung fibrosis
Anthracyclines (e.g doxorubicin)	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy

Antimetabolites

Cytotoxic	Mechanism of action	Adverse effects
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis, lung fibrosis
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis by blocking thymidylate synthase (works during S phase)	Myelosuppression, mucositis, dermatitis
6-mercaptopurine	Purine analogue that is activated by HGPRTase, decreasing purine synthesis	Myelosuppression

Cytotoxic	Mechanism of action	Adverse effects
Cytarabine	Pyrimidine antagonist. Interferes with DNA synthesis specifically at the S-phase of the cell cycle and inhibits DNA polymerase	Myelosuppression, ataxia

Acts on microtubules

Cytotoxic	Mechanism of action	Adverse effects
Vincristine, vinblastine	Inhibits formation of microtubules	Vincristine: Peripheral neuropathy (reversible) , paralytic ileus Vinblastine: myelosuppression
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Topoisomerase Inhibitors

Cytotoxic	Mechanism of action	Adverse effects
Irinotecan	Inhibits topoisomerase I which prevents relaxation of supercoiled DNA	Myelosuppression

Other cytotoxic drugs

Cytotoxic	Mechanism of action	Adverse effects
Cisplatin	Causes cross-linking in DNA	Nephrotoxicity (the primary dose-limiting side effect), Ototoxicity, peripheral neuropathy, hypomagnesaemia
Hydroxyurea (hydroxycarbamide)	Inhibits ribonucleotide reductase, decreasing DNA synthesis	Myelosuppression

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A 53 year old patient has undergone six cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) chemotherapy and is now attending the lymphoma follow up clinic. He complains of an ongoing and unrelenting tingling in his feet and legs as well as his right hand. This is associated with pain in the extremities that is worsened by the cold weather.

Examination reveals normal motor strength throughout all 4 limbs but marked reduction in proprioception in both legs below the knee and also the right hand. The is a 'glove and stocking' distribution of loss when tested for pin-prick sensation and a reduced joint position sense to the ankle in both lower limbs. Plantar reflexes are normal. During the examination you it is noted that the patient has sustained an injury to the sole of foot which he was unaware of.

What is the most likely causative agent for these symptoms?

- Rituximab
- Cyclophosphamide
- Doxorubicin
- Vincristine
- Prednisolone

Submit answer

Reference ranges

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What is the most likely causative agent for these symptoms?

Rituximab	1%
Cyclophosphamide	3%
Doxorubicin	3%
Vincristine	92%
Prednisolone	1%

The symptoms being experienced above are classical for chemotherapy induced peripheral neuropathy. This is a condition that can occur in up to 40% of patients being given chemotherapy with agents such as platinum based drugs (cisplatin and oxaliplatin), vinca alakloids (vincristine and vinblastine), thalidomide and taxanes (paclitaxel and docetaxel). The treatment of chemotherapy induced peripheral neuropathy is difficult with patients having severe problems long after the causative agent has been given. In most cases it is irreversible. The best medication for treatment is gabapentin or pregabalin which should be titrated up to therapeutic levels and used in conjunction with another analgesic agents.

There are ongoing trials aiming to find a prophylactic agent to help prevent this painful sequealae of treatment, but as yet there has been no convincing evidence to suggest any one treatment.

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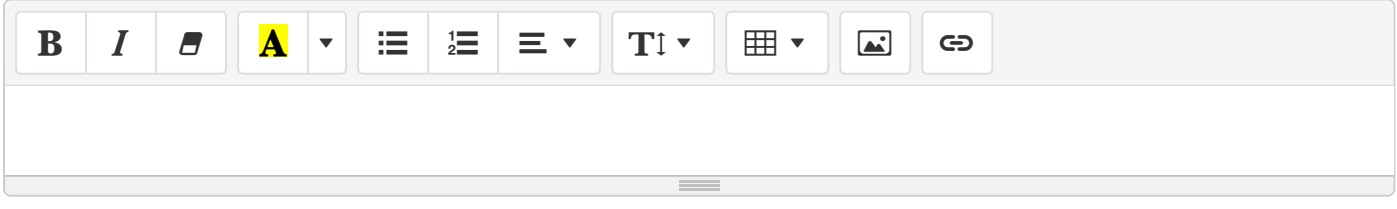

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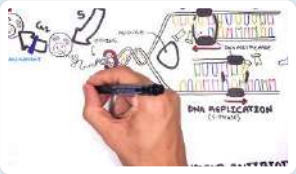

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